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ATELECTATIC OR COMPENSATORY BRONCHIECTASIS

BY

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Historical.

Atelectasis or collapse of the lung as a cause of bronchiectasis is not by any means a recent idea. Reynaud, as long ago as 1835[1], in a comprehensive study of bronchial obstruction, noted that dilatation of the lumen might be present both proximal and distal to the obstruction. The dilatation proximal to the obstruction he ascribed to the increased force of the inspired air held up at the obstruction and that beyond the obstruction he considered was due to the bronchi attempting to fill the space vacated by the collapsed lung.

Some ten years later Hasse[2], in the discussion of bronchiectasis in his treatise on 'Diseases of the Organs of Circulation and Respiration,' expresses the opinion that the condition is invariably due to collapse or shrinkage in size of the lung. A common cause of the collapse he considered obstruction of the bronchus by secretion from an inflamed mucosa. As he says, 'the bronchi become plugged with fibrinous exudation occasioning a collapse of adjacent air cells. The space thus set free is sought to be filled by expansion of the neighbouring parts, giving rise in the majority of cases to emphysema; where, however, the collapse does not occur close beneath the surface of the lung, but at a greater depth and near a large bronchial tube, and where it comprehends a larger tract of pulmonary substance, the result is bronchiectasis.' Hasse attributes the occurrence of bronchiectasis following pneumonia and pleurisy to the same underlying cause, viz.:—the inability of the damaged lung to expand sufficiently to fill the thorax and not, as had been done some years previously (1838) by Corrigan[3], to the contraction of new-formed fibrous tissue. It is interesting to note in passing that Hasse remarks that the variety of bronchiectasis following pneumonia he has met with 'most frequently, in the inferior lobe, especially of the left lung.' Even for bronchiectasis developing in a tuberculous focus at the apex of the lung he suggests the same explanation.

The teaching of Reynaud and Hasse did not receive, however, general acceptance. The majority of authors apparently could not visualize dilatation of the bronchi resulting from collapse unless in consequence of some abnormal positive force, particularly of the nature of increased intra-bronchial pressure. Such had been Laennec's[4] conception of genesis, for in his original description (1819), he ascribed the condition to distension by secretion accumulating within the bronchus. This idea of increased intra-bronchial pressure also underlies the teaching of Stokes (1837)[5] who considered increased expiratory effort, as in coughing, the true aetiological factor. On the other hand, Corrigan as just mentioned, saw the abnormal

force acting from without and caused by the contraction of inter-bronchial, new-formed fibrous tissue.

Curiously, that astute physician, W. T. Gairdner (1850-51)[6], in a critical survey of the ' Consequences of Bronchitis,' while concluding that emphysema results from an attempt on the part of one portion of the lung to fill a space in the thorax previously occupied by some other portion of the lung, and is thus truly complementary, absolutely denied that the same factor could be responsible for the inception of bronchiectasis. It was presumably the fact that bronchiectasis is often localized, and at the same time is saccular in nature, which prevented him from accepting the view of Hasse, although this author had quite unequivocally stated that tubular and saccular dilatations were met with in the same portion of the lung and therefore could not be taken as evidence pointing to any particular aetiology. The primary cause of bronchiectasis Gairdner considered some local weakness of the bronchial wall and he concluded that the dilatations were ' the result of excavations of the lung communicating with the bronchi.' He admitted that once they have originated as ulcerative cavities they might become ' afterwards expanded beyond their original dimensions by inspiratory force.'

The view that pulmonary collapse did play a part in the aetiology of bronchiectasis nevertheless did continue to receive some support. Thus Bastian in 1870[7], while opposing the teaching of Corrigan that cirrhosis of the lung is invariably accompanied by, or invariably accompanies bronchiectasis, mentions that dilatation of the bronchi may be compensative in nature, although his phraseology reveals a certain confusion of thought regarding its modus operandi. He says, ' It is obvious that something must go towards filling up the space left by the shrinking lung, and if displacement of viscera does not take place, then the bronchi must yield and dilate in some of their weakest parts under the continually increasing pressure of the inspired air.'

The dilatation is undoubtedly due to the inspiratory efforts but not because of a rise in the intra-bronchial pressure. Inspiration acts by increasing the capacity of the thorax which, as Nature abhors a vacuum, must be filled and this can only occur by dilatation of any spaces in communication with the external air. Normally the air cells provide for this but when these are not available, as in the state of collapse, then the bronchi must take their place. This point of view is clearly expressed in the recent article on ' Dry bronchiectasis ' by Wall and Hoyle[7a]. The conception of respiration acting through an increase in the intra-bronchial pressure is due to a want of appreciation of the physical conditions during inspiration and expiration and is being continually encountered in the discussions of both emphysema and bronchiectasis not only in the works of the earlier writers but even in some of most recent date (McCallum[8]). The inspired air enters by suction and hence during this phase of respiration there is in reality always a diminished pressure within the bronchi. On the other hand, during expiration the intra-bronchial pressure may be raised but it is most improbable that this can have any dilating effect, since the bronchi are amply supported by the surrounding lung and other thoracic tissues. As Hedblom[9] puts it, the force which would cause increased intra-bronchial pressure is applied to the outside of the bronchi.

An important date in the history of bronchiectasis is 1885. In that year Heller[10] published a communication entitled, ' Die Schicksale

atelektatischen Lungenschnitten,' in which dilatation of the bronchi was referred to as a sequel of congenital atelectasis and in which we find the term ' atelectatic bronchiectasis '* employed for the first time. Until this date all writers had recorded bronchiectasis consequent on collapse of a lung previously air-filled, and thus it is not surprising that the condition had never been referred to as atelectatic bronchiectasis because such a designation would not be correct etymologically. For this very reason not a few at the present moment object to the term as employed to-day because no one, not even those who most frequently use it, believe that congenital atelectasis is a common cause. A term which would be more strictly correct, and which would apply equally to dilatations consequent on atelectasis or collapse of the lung is ' compensatory bronchiectasis ' and hence it is used as an alternative in the title of the present article.

Heller in his paper describes severe bronchiectasis in several patients dying between the ages of nine months and seven-and-a-half years which he considered as the sequel of congenital atelectasis because of the situation of the lesion, the absence of pigment and the histological appearances. Like Laennec, and in contrast to most present-day observers, Heller found the condition most frequent in the upper lobes. He says it usually involves a whole lobe (most seldom the middle and lower lobes) which is pale, smaller than normal and composed of many pus-containing cavities separated by narrow septa devoid of anything suggesting lung tissue. It is the absence of pigment and alveolar spaces which caused Heller to consider the condition due to changes ensuing in pulmonary tissue which had never expanded. Heller does not discuss the way in which he believes the bronchial dilatation comes about but simply contents himself with recording its occurrence and describing the appearances, naked-eye and microscopic. He does say, however, that he is doubtful if the same results would ensue in lung which had become secondarily atelectatic because the cause of the post-natal collapse would most probably bring about other changes in the lung.

Other writers who have described cases of bronchiectasis which they considered due to congenital atelectasis are Lutmar (1908[11]) and Buchmann (1911[12]). Lutmar records two examples of atelectasis, involving the left and right lower lobes respectively. In both the pulmonary tissue was shrunken, the alveoli were collapsed but not obliterated, and there was much new-formed fibrous tissue around the bronchi but it was only in the example implicating the left lower lobe that bronchiectasis was present. Although pigment was present in the shrunken right lower lobe Lutmar did not consider this fact inconsistent with a diagnosis of congenital atelectasis.

Buchmann described five examples of pulmonary collapse with bronchiectasis discovered post mortem in patients dying between the ages of forty-nine and eight-four years. In two of the patients both upper lobes were involved, in one an upper lobe only and in two the left lower lobe was the seat of the mischief. It is interesting to note that while Lutmar ascribed no significance to the presence of pigment as indicating whether the pulmonary collapse was congenital or acquired, Buchmann, like Heller, considered this a most important differentiating feature. For example, in one of his patients with bilateral disease involving each upper lobe pigment was present on one side and not on the other and in consequence he concluded that the condition was due to acquired collapse and congenital collapse respectively.

* Heller used the expression " Atelektatische Bronchiecktasien."

In spite of communications such as the above, pulmonary atelectasis (either congenital or acquired) was not accepted by the majority of writers as an important factor in the causation of bronchiectasis. Most writers during the latter part of the last, and the first quarter of the present century give it scant notice, although it should be mentioned that D. J. Hamilton was a notable exception when he wrote in 1894 that ' pulmonary collapse is a fertile source of bronchiectasy in children.'[13] Within the last decade, however, pulmonary collapse as a cause of bronchiectasis has become increasingly stressed until at the present moment it would appear to be the most popular theory of aetiology. This change in opinion is not due to any fresh pathological evidence, nor is it because of a better appreciation of the clinical manifestations of the disease, but depends almost entirely on the view that a triangular shadow in the skiagram and situated at one or other diaphragmatico-vertebral angle invariably spells collapse of the lung.

The triangular shadow.

It is a general law in radiology that any abnormal appearance may be caused by several distinct pathological conditions and it would be remarkable if the so-called triangular shadow formed an exception to this rule. This is, however, not the case for there are at least four different pathological lesions which can give rise to a wedge-shaped shadow occupying one or other diaphragmatico-vertebral angle.

1. Mediastinal pleurisy.—There is no doubt that a radiological shadow, of a somewhat triangular shape with a sharply defined outer margin and situated in one or other diaphragmatico-vertebral angle, may be produced by an accumulation of fluid (usually purulent) in the mediastinum or its neighbourhood. This was first pointed out by Savy[14] who remarked that it resembled the appearance caused by a pericardial effusion. This would suggest that the outer margin would have a convex contour and, as a matter of fact, inspection of the various diagrams illustrating Savy's paper shows that the hypotenuse of the triangle is invariably convex. This is what would be expected, especially if the fluid were under pressure.

Although there have been recorded not a few supposed examples of this condition since the first description of Savy in 1910, it is questionable if they were all of this nature. In only a small proportion of the cases was the presence of fluid confirmed either by exploration or at autopsy, and it is only in those so verified, as for example, in the one recorded by Wallgren[15] (fig. 1), that the skiagram revealed a convex hypotenuse. In the cases in which the diagnosis was not verified, and this obtains as we have already remarked in the majority of published reports, the hypotenuse of the triangle was straight or even concave so that in all probability the pathological lesion was of a different nature. It must be pointed out, however, that a convex hypotenuse, although essential for a diagnosis of fluid, does not necessarily indicate that this is the nature of the lesion. In one personally observed example of unequivocal pulmonary collapse, in which reinflation of the lung

caused the immediate disappearance of the shadow, the hypotenuse was definitely convex (fig. 4).

Assmann[16], while discussing mediastinal pleurisy, says that in his experience the lesion causing this radiological appearance is more frequently cicatricial in nature due to tuberculosis of the mediastinal glands or more rarely following pneumonia. Assmann speaks of the hypotenuse being concave so that he certainly was not dealing with an accumulation of fluid. That pleural thickening and mediastinal fibrosis may explain some of the triangular-shaped shadows is not improbable, since we have recently observed the persistance of a typical triangular shadow in a case of bronchiectasis after removal by lobectomy of a supposed atelectatic lobe.

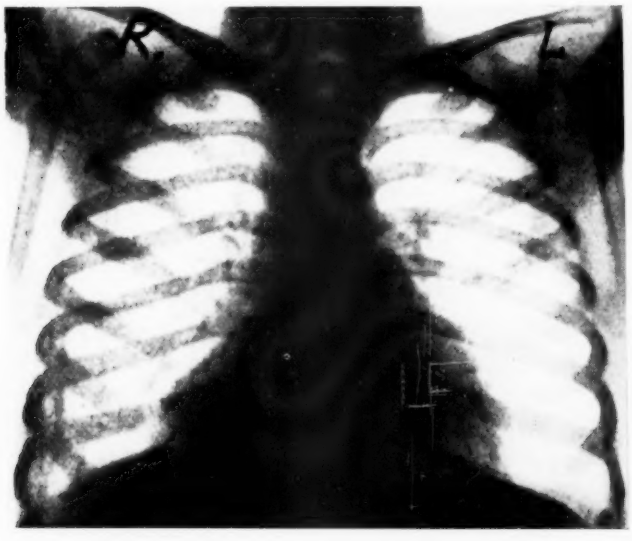

FIG. 1.—Skiagram in case of mediastinal pleurisy on right side recorded by Wallgren. Note the convex contour of triangular shadow in right vertebro-diaphragmatic angle. The chest was explored and 20 c.c. straw coloured, serous fluid removed. [From Beiträg, z. Klinik d. Tuberkulose, 1928, LXIX, 641.]

2. Fibrosis of lung.—In 1927 Rist, Jacob and Trocemé[17] recorded five cases in which a triangular shadow in the diaphragmatico-vertebral angle was not due to a collection of fluid but to fibrosis of the lung with bronchiectasis. It is interesting to note that in three of the patients the radiological appearances were responsible for a diagnosis in the first instance of a mediastinal pleural effusion.

One typical example of the series is that of a girl aged twenty years who had a cough and purulent sputum with occasional haemoptysis since an attack of measles at the age of two years. She came under observation during an acute exacerbation with fever, haemoptysis, severe cough and foetid sputum, and at this time x-ray examination revealed a triangular shadow at the right base. Although the published reproduction of the x-ray picture referring to this case in the series shows the hypotenuse to be concave, a diagnosis of purulent mediastinal pleurisy was made. However, on exploration of the

chest by operation, no pus was discovered but a much fibrosed lung, and a lipiodol injection at a later date disclosed bronchiectasis.

In spite of the fact that Rist and his colleagues demonstrated at operation that the lung was fibrosed and firmly adherent with a much-thickened pleura these cases have been not infrequently quoted by subsequent writers as examples of atelectasis with bronchiectasis.

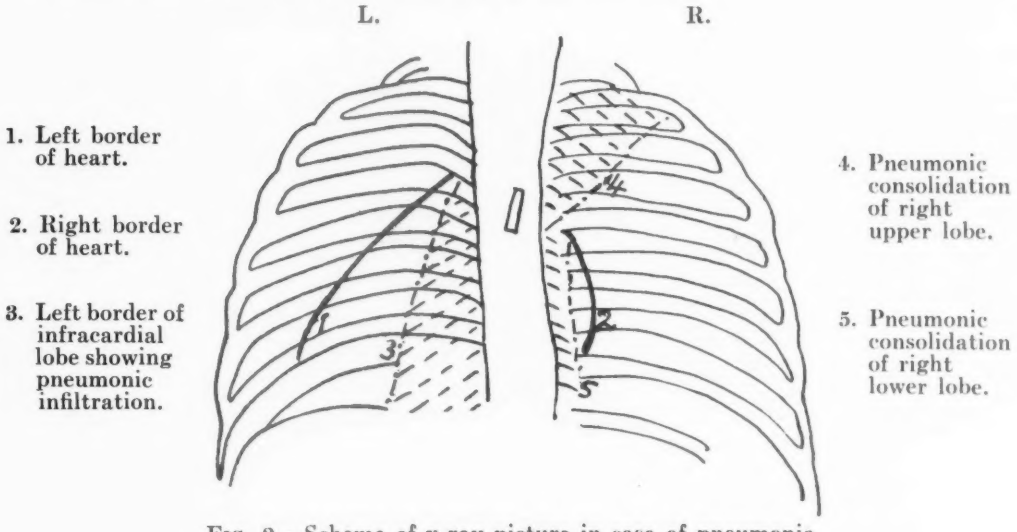
L.
R.
1. Left border of heart.
2. Right border of heart.
3. Left border of infracardial lobe showing pneumonic infiltration.
4. Pneumonic consolidation of right upper lobe.
5. Pneumonic consolidation of right lower lobe.

FIG. 2.—Schema of x-ray picture in case of pneumonia recorded by Ettig. [From Monatsch. f. Kinderheilk., 1924, XXVIII, 209.]

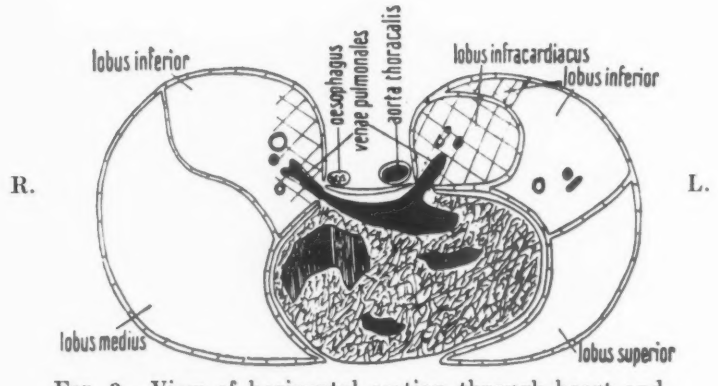

FIG. 3.—View of horizontal section through heart and lungs on level with lower part of root of lungs seen post-mortem in case of pneumonia recorded by Ettig. [From Monatsch. f. Kinderheilk., 1924, XXVIII, 211.]

3. Pneumonia.—A triangular shadow may also be caused by acute pneumonic consolidation. In this condition the hypotenuse is straight. Such a finding has been described by Gullbring[18] and Ettig[19] in two instances in which the diagnosis was verified by post-mortem examination. In Ettig's patient, it is interesting to note, the pneumonia involved an accessory (infracardiac) lobe (fig. 2 and 3). Considering how frequently a complete

lower lobe is affected in pneumonia, it is indeed remarkable how seldom such a radiological picture is observed. The only pneumonic consolidation which is commonly accompanied by a sharp margin to the radiological shadow is that involving the right upper lobe when the sharply defined lower and horizontal border is ascribed to the presence of an interlobar pleural exudate. The same accumulation of exudate must take place frequently between the upper and lower lobes, but in these circumstances the layer of exudate is not seen ' end on,' as is the case when it is present in the fissure between the upper and middle lobes, but rather ' on the flat,' and it may be for this reason that it seldom casts a shadow in the radiogram.

4. Collapse of the lung (atelectasis).—I do not know who was the first to suggest that this peculiar and characteristic shadow might be caused by pulmonary collapse but the earliest indication that I have come across is to be found in a paper by Singer and Graham[20] entitled ' The roentgen-ray study of bronchiectasis.' These authors state that in some cases operated upon the triangular shadow had been found to be due to atelectatic and bronchiectatic lobes.

There is no doubt that a triangular shadow situated in one or other diaphragmatico-vertebral angle may arise from pulmonary collapse[21]. I have seen several examples in which atelectasis was unequivocally the cause of the x-ray appearances because inflation of the lung brought about a rapid disappearance of the shadow. It should be noted, however, that when the shadow results from collapse of the lung the hypotenuse of the triangle may be convex, straight or concave. This variation in the radiological picture probably depends on the amount of air left in the lung. But whatever the explanation, this fact renders its differentiation from the other types of lesion by radiological means alone impossible. The only criterion by which it can be decided that a particular shadow in the skiagram is due to collapse of the lung, at least during life, is the ability to cause its rapid and complete disappearance by re-inflation. This is the acid test and may be applied by any means which brings about forced and deep breathing. The method which I have generally adopted is the inhalation of carbon dioxide in oxygen.

It is worthy of comment that a sharply defined triangular shadow is never observed in the case of the pulmonary collapse (so-called massive collapse) which occasionally ensues after abdominal or thoracic operations. This only makes it all the more striking that it should be such a constant picture in the case of spontaneous pulmonary collapse in the child. It is just possible that this difference is due to the fact that in the former the condition is not limited to one lobe but invades the whole lung or at least the greater part of one lung. Graberger[22], while discussing this very point, says that the only conditions which give a sharply defined shadow radiologically are encapsulated exudates or pneumonia which extends to a fissure, and at the same time he raises the question of some of the shadows being

due to disease of an accessory lobe. He would explain the smaller shadows in this way. Such an assumption, however, seems quite unnecessary since in those cases in which the whole lower lobe was known to be involved in the disease (pneumonia or atelectasis) the size of the shadow in comparison with that of the lobe itself seems relatively small.

The presence of an accessory lobe is quite a common condition in the lower animals and in the ape and is not unknown in man. Kerley[23], following the teaching of Schaffner[24], has stressed the frequency of the accessory lobe in man, especially on the right side, and says that it is present in 40 per cent. of individuals. In my post-mortem experience an accessory lobe is a rare finding and Schonfield[25] records that he only observed the condition once during the course of several years' post-mortem examinations. Kerley also makes the statement that this abnormality of the lung is a potent factor in the causation of bronchiectasis but he gives no reason why he has come to this conclusion. One feels that the frequency with which the bronchiectatic condition extends into the neighbouring lobe is rather against such a view. Further, it is difficult to reconcile this aetiological factor, which Kerley and all writers admit occurs most often on the right side, with the predilection of bronchiectasis for the left side. The frequent occurrence of bronchiectasis at the left base, however, is one of the most difficult features to account for by any explanation of the pathogenesis of the disease.

Atelectatic bronchiectasis.

Within recent years there have been published not a few cases of so-called atelectatic bronchiectasis but unfortunately in not one is it certain that this diagnosis was correct. For the most part the diagnosis depended simply on the presence in the skiagram of a triangular shadow in association with bronchiectasis. It has been indicated that this shadow may be produced by several different pathological lesions and not only by atelectasis. During life, and it may be noted that practically all the published cases were observed during life, the only way to be certain that the shadow is due to atelectasis is, as already mentioned, its immediate disappearance on re-inflation of the lung. This, according to the authors, was attempted in several of the patients but in not one instance did it meet with success.

An oft-quoted example of atelectatic bronchiectasis is that published by Sparks[26] in which the shadow did disappear, but it should be noted that this was spontaneous and not in response to any measure which had been adopted. This case was recorded under the title of 'An unusual case of bronchiectasis.'

The patient was a girl of twenty-two years who had pneumonia at the age of seven years and ever since then had suffered from recurrent attacks of bronchitis and symptoms of asthma. On coming under observation physical examination revealed flattening and relative dulness with a deficient

respiratory murmur on the left side of the chest and fine, sticky crepitations at the base. X-ray examination at this date demonstrated a triangular shadow at the left base. Some time later, exactly how long is not stated, and immediately after the injection of lipoidol, the triangular shadow had disappeared but a severe degree of bronchiectasis was demonstrated in the situation which had been occupied by the shadow. Unfortunately in the print published all the lipoidol is in the right (healthy) lung. However, at a still later date, injection of lipoidol was repeated and the accompanying print of the skiagram does reveal a severe degree of bronchiectasis in the left lower lobe.

It is quite possible that the triangular shadow in Spark's case was due to pulmonary collapse, but it is by no means certain that this was so. The radiological appearances could equally well be due to pneumonia. But what is most unlikely is that the pulmonary collapse, if indeed it were such, had any aetiological significance for this would mean that it had been present for sixteen years (the symptoms having been present since the patient was seven years old) and that at the end of this time the lung had been capable of complete re-inflation while the severe bronchiectatic condition persisted. One does know that the lung may be kept collapsed by means of an artificial pneumothorax for several years and yet suffer no damage, but one would have thought that after a period of sixteen years the atelectatic lung would have undergone fibrosis. Hence, if the shadow were caused by pulmonary collapse, it in all probability was an intercurrent event. There was also lacking the acid test—the immediate disappearance following attempts to re-inflate the lung. It might be argued that a failure to cause the shadow to disappear by re-inflation did not necessarily indicate that the condition was not due, at least in the first instance, to collapse. After a time the collapsed lung becomes fibrosed so that its re-expansion is impossible. This possibility has indeed been suggested by Ellis[27], and, as he remarks, makes it exceedingly difficult to draw definite conclusions.

One naturally thinks of pathological evidence as the best means of determining the nature of the lesion. This type of evidence, however, has serious limitations since, as a rule, it is only obtainable many years after the onset of the mischief, when time has been given for secondary changes to set in and ample opportunity for superimposed inflammation, so that it is difficult to unravel the story of events. So far as I am aware there has been only one example of supposed atelectatic bronchiectasis submitted to post-mortem examination within recent years and in this no minute histological examination was carried out[28]. One should perhaps include in this category the examples quoted by Singer and Graham[29] which were removed at operation, but here again histological evidence is wanting. In any case, it would seem from the available descriptions[29] that the changes supervening in the atelectatic lung closely simulate those which follow inflammation, so that the end-results in atelectasis and unresolved pneumonia are indistinguishable. The great desideratum at the present moment is minute investigation of material obtained earlier during the course of the disease and it is to be

hoped that the operation of lobectomy, which is becoming more popular, will supply an opportunity of which full advantage will be taken. In the meantime it would seem wise to reserve judgment regarding any particular example of bronchiectasis ascribed to collapse of the lung unless there is proof of the lung being re-inflatable.

One does not deny the possibility that some of the cases above referred to, and others appearing in the literature, were examples primarily of pulmonary collapse with compensatory bronchiectasis. The view held is that in none of them has it been shown that collapse of the lung had ever occurred and hence that this lesion had played any part in the production of the

FIG. 4. Case 1.—Pulmonary collapse. Skiagram showing dense triangular shadow in right diaphragmatico-vertebral angle with convex hypotenuse.

bronchial dilatation. In all of them there must have been fibrosis, otherwise the lung could have been inflated. The fibrosis itself, which it must be remembered has several causes, could account for the bronchietasis. At any rate, it would appear in view of the cases recorded below that it is a subsequent fibrosis or cirrhosis of the lung, whatever its cause, which not only hinders the bronchial tree from returning to its normal state but which also increases the abnormality. At least when I have been able to demonstrate by causing re-inflation of the lung that atelectasis or pulmonary collapse really was present, any bronchiectasis which existed was slight in extent and was completely recovered from. The following case is such an example.

Case records.

Case 1. A. R., a boy, first came under observation at the age of eight years in March, 1932. He had had a healthy infancy and had remained well till he was aged five years when he suffered from an attack of pneumonia. Since then he is reported ' never to have been the same, to be puny and undersized and frequently ailing.' There was no history of sputum. Three months previously there developed considerable enlargement of the cervical glands on the left side which, however, had largely but not entirely disappeared. The tonsils had been removed at the age of six years.

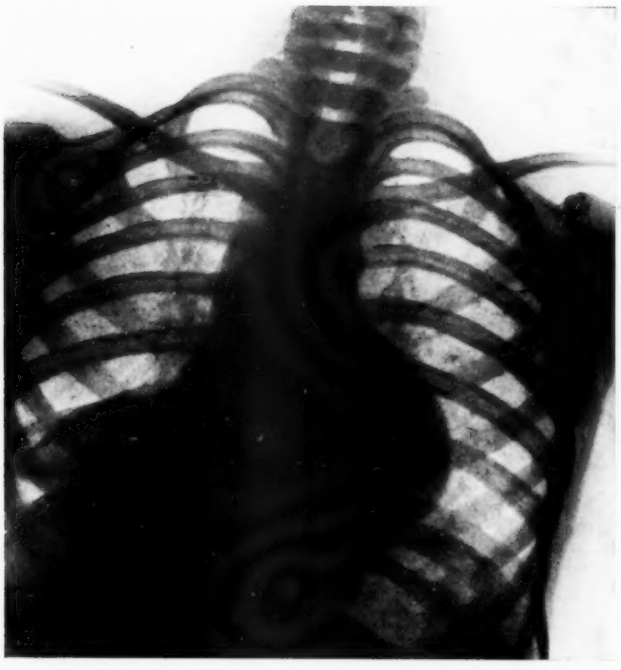

FIG. 5. Case 1.—Pulmonary collapse. Skiagram immediately after the inhalation of carbon dioxide in oxygen. Note that the shadow is less dense and has retracted from chest wall and diaphragm. Compare with fig. 4.

Three weeks before coming under observation he had contracted measles. The attack was uncomplicated, but because the Mantoux tuberculin test was strongly positive he was referred to me for observation. At this time (March, 1932) he was definitely underweight (weighing 43 instead of 55 lb.), he complained of a troublesome cough at night but with the exception of some enlargement of the glands on the left side of the neck and a slight degree of rhinitis, nothing abnormal was detected on physical examination. The boy was given tonic treatment and recommended for a period at a convalescent home.

Although he increased in weight the cough persisted. In August, 1932, the Mantoux test was strongly positive. On September 7, the house physician, during his routine examination, detected for the first time some impairment of the percussion note at the right base behind with tubular breath sounds and x-ray examination of the chest revealed a definitely abnormal and unusual picture (fig. 4). There was at the right base a shadow,

FIG. 6. Case 1.—Pulmonary collapse. Skiagram after intratracheal injection of lipiodol showing a moderate degree of dilatation of the main branches of the bronchial tree supplying the right lower lobe.

convex and sharply defined above and merging below with the liver shadow. I saw the child on October 5, when it was noted that expansion of the right chest was defective and that the percussion note was impaired all over the right side with definite dulness at the base behind where

the breath sounds were tubular in character. On screening, the shadow at the right base, was observed to be very dense, to be sharply defined above, and to be continuous below with the diaphragm which was immobile. A provisional diagnosis of pulmonary atelectasis was made and the boy was admitted to hospital for investigation.

On October 11, after one week in hospital, the following note was made: ' Patient is quite comfortable but has a troublesome cough. There is no sputum and no fever. The pulse which on admission was 110 has during the last three days declined to between 60 and 70. Movement of right side of chest is still defective. Note over right side is generally of higher pitch but definitely dull at base behind, where the breath sounds are deficient. Shadow in skiagram at right base if anything less dense but still very distinct.

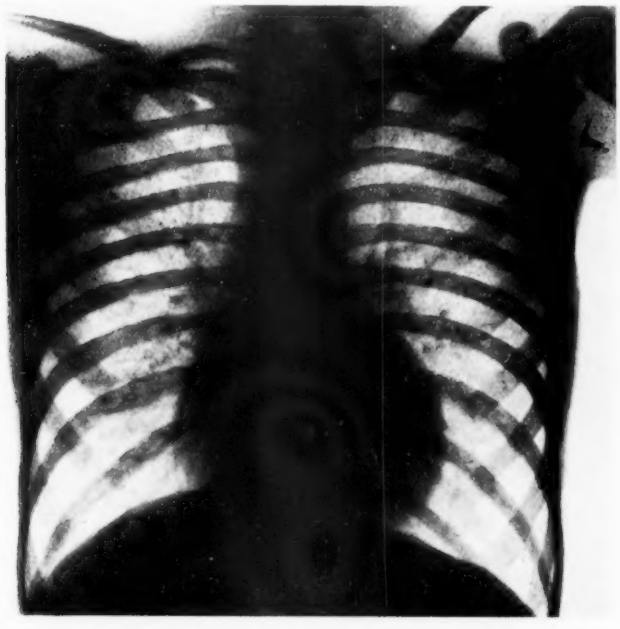

FIG. 7. Case 1.—Pulmonary collapse. Skiagram of chest taken six minutes after disappearance of triangular shadow and showing normal lung fields. [2.V.33.]

In order to test the question of atelectasis inhalation of carbon dioxide in oxygen was practised. The child became cyanosed, breathed deeply and was rigid (? tetany) and excitable for a short period. A skiagram taken afterwards revealed the shadow practically unchanged. On October 14, an inhalation of carbon dioxide in oxygen was again resorted to. On this occasion there did result a change in shadow (compare fig. 4 before and fig. 5 after inhalation of carbon dioxide). In fig. 5 the shadow seems less dense and more retracted from the chest wall. As the cough persisted and the shadow had not absolutely disappeared

it was decided to give a lipoidol injection. This was done on October 18, and revealed a definite though slight degree of bronchiectasis (fig. 6). In this picture the shadow seemed to have disappeared.

The patient was recalled in May, 1933, six months after the last examination. In the interval he had been quite well with

FIG. 8. Case 1.—Pulmonary collapse. Skiagram after intratracheal injection of lipiodol showing disappearance of bronchiectasis.

only an occasional cough. Expansion of the right chest seemed still deficient and after inversion of the child, producing cough without any sputum, the breath sounds assumed a questionable tubular quality at the angle of the right scapula where the whispered voice was unduly distinct but not to the extent which had been present before. X-ray examination of the chest at this time did not reveal any shadow (fig. 7) and after injection of

lipoidol there was no evidence of the previous bronchiectasis, the bronchi having quite regained their normal conformation (fig. 8).

Another probable example of atelectatic bronchiectasis is the following (case 2), although in this instance re-inflation of the lung was not attempted. The patient was one of a series which Dr. Stanley Graham and I reported in an earlier issue of this Journal during a discussion of the ' Prognosis in bronchiectasis '[30]. At that time I did not appreciate the full significance of the triangular shadow and considered that it only betokened fibrosis of the lung. But in view of the preceding case I decided to review afresh all those in

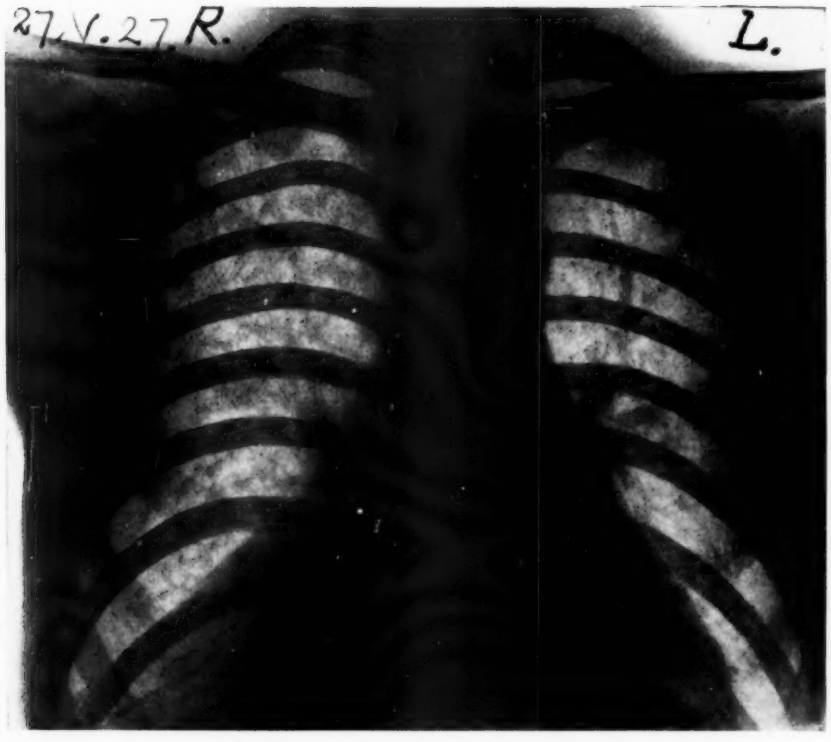

FIG. 9. Case 2.—Possible pulmonary collapse. Skiagram showing triangular shadow at either base, that on right side having a convex contour. [27.V.27.]

which I had seen recovery from bronchiectasis take place and especially those in which a triangular shadow had been present.

In this particular instance the shadow disappeared spontaneously and thus might have been due to an intercurrent pneumonia but its presence at either base, the sharply defined margin which was convex on one side (fig. 9), the absence of fever and the history of a severe uncontrollable cough which

seems specially characteristic of pulmonary collapse, and the complete disappearance of the bronchiectasis make it in all its features practically identical with the preceding case.

Case 2. (Case 10 of original series[30]). A. S., a boy, came under observation on May 25, 1927, when aged twelve-and-a-half years, with a history of cough with sputum of three months' duration. At the age of two years he had passed through an illness comprising measles, whooping cough and pneumonia, but he apparently made a good recovery and had remained in good health till the onset of the present illness. The cough had steadily got worse and was often severe enough to cause vomiting. There was impairment of the percussion note at both bases behind with somewhat tubular breath sounds and x-ray examination revealed a triangular-shaped

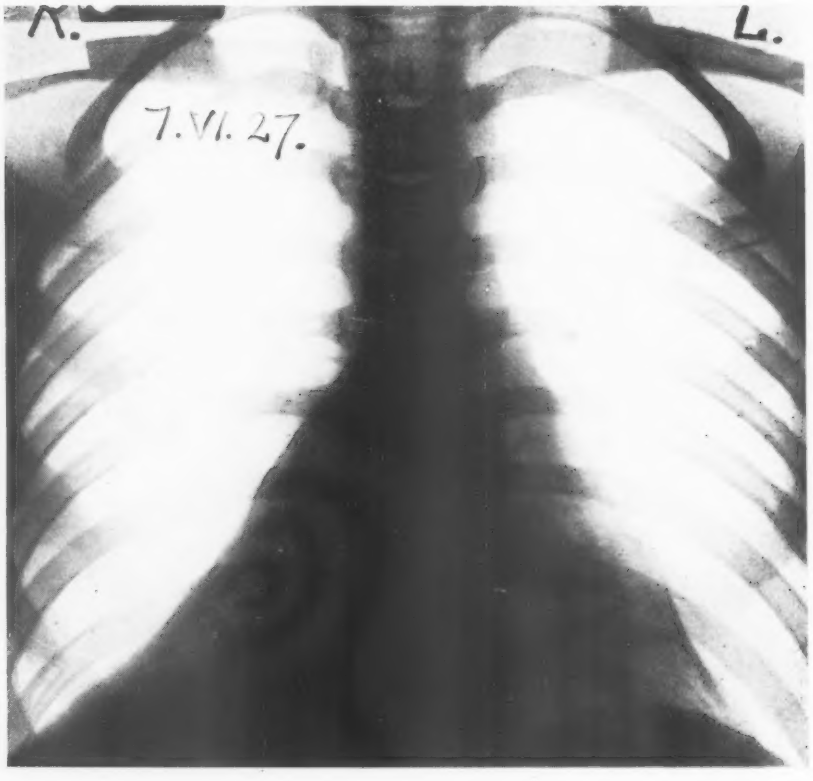

FIG. 10. Case 2.—Possible pulmonary collapse. Skiagram taken 10 days after fig. 9, showing disappearance of shadow at left base and increase in density of shadow at right base, which has now lost convex contour. [7.VI.27.]

shadow at either base. The shadow was less dense on the right side but had a convex contour while on the left side the hypotenuse of the triangular area was straight. A provisional diagnosis of pulmonary fibrosis with possible bronchiectasis was made and the boy was admitted to hospital for investigation.

On admission, June 7, he was described as a big well-nourished boy, 152 cm. tall and weighing 29·5 kgrm. Examination of the chest at this date revealed impairment of the percussion note only at the right base behind where the breath sounds were amphoric in quality and whispering pectoriloquy was well heard close to the midline. At the same time a skiagram showed the shadow still present at either base, less dense at the left base but

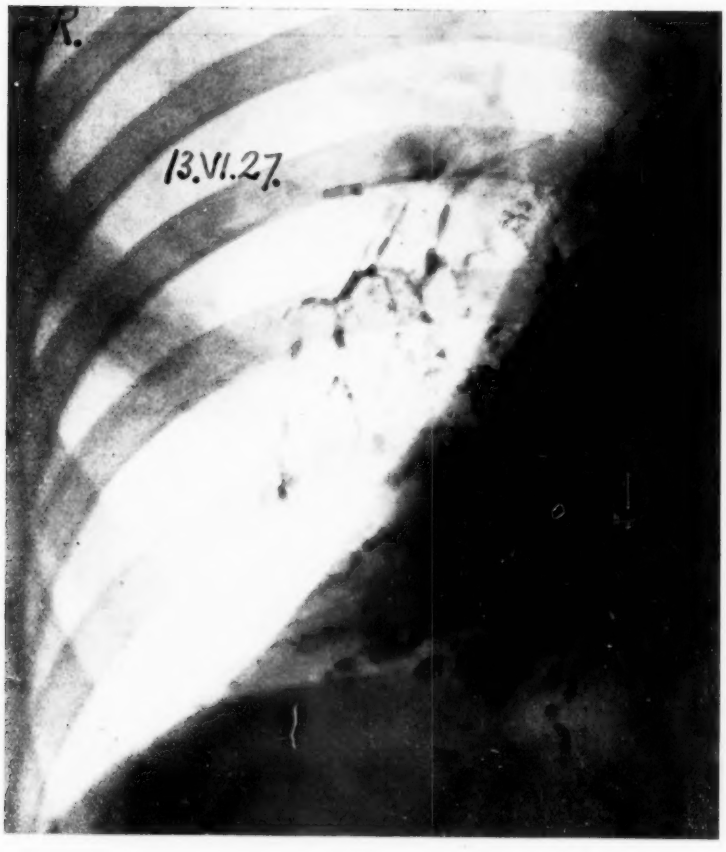

FIG. 11. Case 2.—Possible pulmonary collapse. Skiagram after lipiodol injection showing slight degree of dilatation of bronchi of right lower lobe, which are bunched together in the zone of the triangular shadow. [13.VI.27.]

more dense on the right side with the hypotenuse now straight (fig. 10), and after the injection of lipiodol a definite but moderate degree of dilatation of the bronchi (fig. 11). This finding at the time was taken to corroborate the diagnosis of fibrosis with bronchiectasis, the now-apparent significance of the disappearance of such a shadow not being appreciated.

On April 3, 1930, two years and nine months later, and when the boy was fifteen-and-a-half years of age, he was again seen.

He appeared in perfect health, and the cough and sputum had entirely disappeared. His height was 167·5 cm. and his weight 48·5 kgrm. Examination of the chest still revealed a very slightly impaired percussion note with deficient breath sounds at the right base, but neither amphoric breathing nor pectoriloquy was audible. A skiagram after a lipoidol injection showed that the bronchi were normal in their conformation and there was no suggestion of the previously noted triangular shadows (fig. 12).

FIG. 12. Case 2.—Possible pulmonary collapse. Skiagram after lipiodol injection showing return to normal distribution and conformation of bronchi of right lower lobe, which had been seat of bronchiectasis 3 years previously. [3.IV.30.] Compare with fig. 11.

Dr. Stanley Graham kindly saw the patient for me in February, 1934, when he reported that he was a big, well-developed youth, with neither cough nor sputum and that on x-ray examination of the chest nothing abnormal was detected except a line on either side radiating from about the level of the sixth vertebra to the middle of the diaphragmatic arch and indicating possibly the presence of supernumerary lobes.

In still another case of the series which Dr. Graham and I reported in 1931, the question of collapse of the lung as a factor in the production of bronchiectasis must be considered. In this case also there was a shadow situated at the right base, but it simulated more what is met with in pneumonia than in pulmonary collapse, there being an absence of the triangular shape with a sharply defined outer margin (fig. 13). I personally incline to the diagnosis of pneumonia in this case which is all the more probable as the boy came under observation during a febrile illness. Nevertheless, it may be that the physical conditions which led to the dilatation of the bronchi in these circumstances, were, as originally suggested by

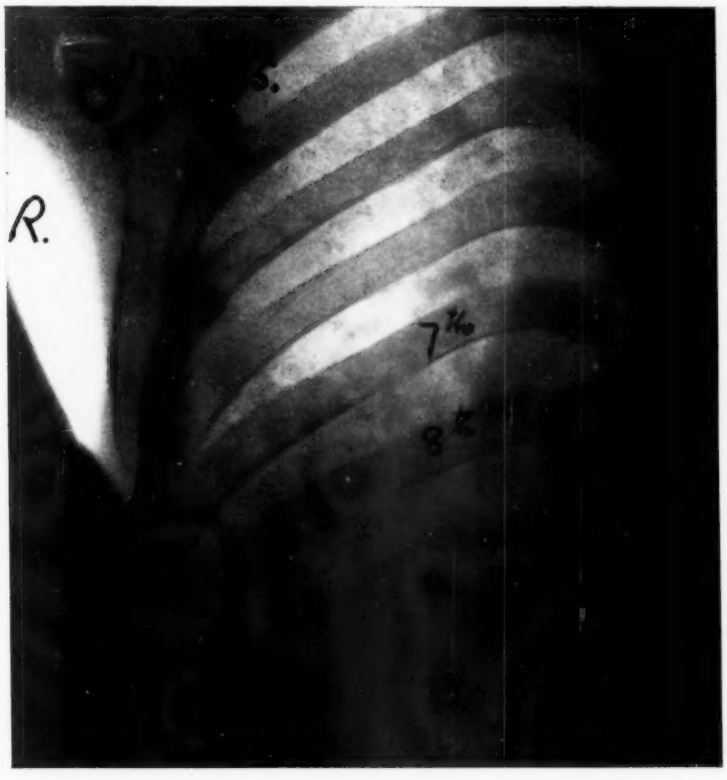

FIG. 13. Case 3.—Skiagram showing consolidation of right lower lobe. [17.VIII.25.]

Hasse, fundamentally the same, viz., the inability of the consolidated lung to expand and fill the thorax so that compensatory dilatation of some air-containing space must result. In any case, it is interesting to note that with the disappearance of the physical signs and radiological manifestations of the condensed pulmonary tissue the bronchi returned to normal dimensions and it would therefore seem appropriate that the case record should be incorporated in this communication.

Case 3. (Case 5 of original series[30]). J. F., a boy, first came under observation in August, 1925, when he was aged nine years. He

had had influenza at three and measles and whooping cough at four years of age, since when he had been troubled with a cough and subject to febrile attacks. It was during one of these febrile periods that he came under observation. At this time he was

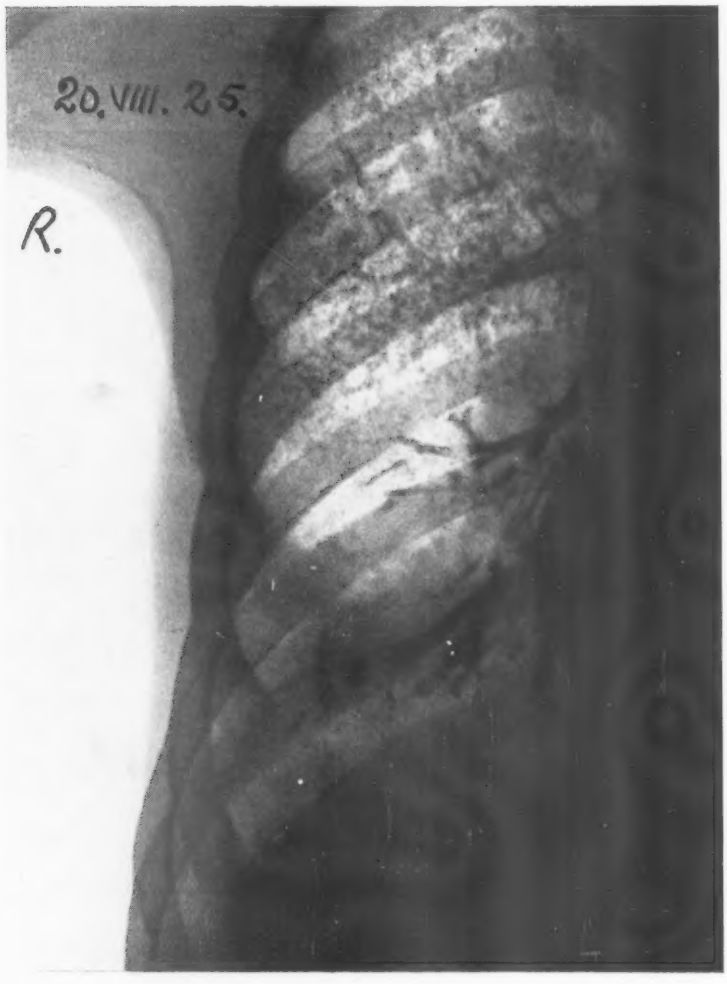

FIG. 14. Case 3.—Skiagram after lipiodol injection showing slight degree of bronchiectasis in right lower lobe. [20.VIII.25]

noted to be an undersized boy measuring 108 cm. and weighing 17·2 kgrm. His colour was good and there was no clubbing of the fingers. The Pirquet tuberculin reaction was positive. Examination of the chest gave a percussion note which was dull with deficient breath sounds at the right base behind below the angle

of the scapula. When the child was made to cough while in the inverted posture one drachm of thick purulent sputum, devoid of all odour, was evacuated and the dulness at the right base became less intense and the breath sounds tubular in quality. X-ray examination revealed widening of the mediastinum and a diffuse mottled shadow at the right base (fig. 13). After the

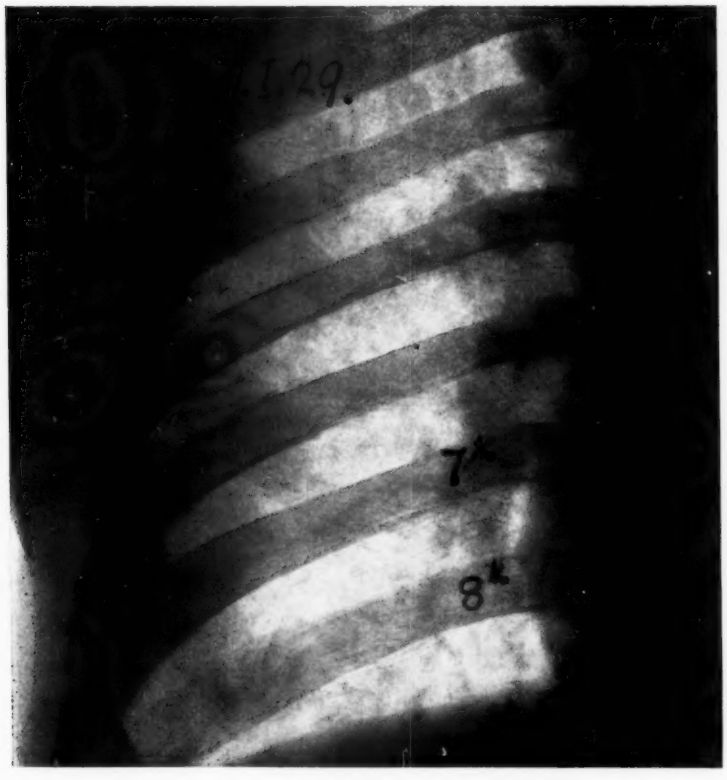

FIG. 15. Case 3.—Skiagram showing chest clear. [31.I.29.] Compare with fig. 13.

injection of lipoidol a slight but definite degree of dilatation of the bronchi was evident in the situation occupied by the above-mentioned shadow (fig. 14).

The boy was seen again in January, 1929, when his health was said to be satisfactory and he was eating and sleeping well and playing normally. He still had a cough but there was no sputum. The physical signs were negative.

On March 28, 1930, four-and-a-half years after first coming under observation, he still looked well but had a dry unproductive

cough. Physical examination was negative and skiagrams of the chest before and after the injection of lipoidal revealed no evidence of the shadow previously present at the right base or of the dilatation of the bronchi which had been noted in the same situation (fig. 15 and 16).

FIG. 16. Case 3.—Skiagram after lipiodol injection showing disappearance of bronchiectasis which had been present 3½ years previously. [9.II.29.] Compare with fig. 14.

Summary.

(1) The history of atelectasis (congenital and acquired) in the production of bronchiectasis is reviewed.

(2) The view that the bronchiectasis accompanying pulmonary collapse is compensatory in nature is supported. The specific cause is the inability of the lung to fill the thoracic cavity and hence the necessity for some space communicating with the external air (alveolus or bronchus) to dilate.

(3) The significance of the so-called triangular shadow in the skiagram occupying one or other diaphragmatico-vertebral angle is discussed. This shadow is shown to be caused by encysted effusions, fibrosis of the lung and thickened pleura, pneumonic consolidation, and collapse of the lung. Stress is laid on the re-inflatability of the lung as essential for a diagnosis of pulmonary collapse.

(4) Some previously recorded cases of atelectatic bronchiectasis are considered and the correctness of the diagnosis submitted to criticism.

(5) Three personally observed examples of bronchiectasis with an accompanying triangular shadow are described. In all the bronchietatic lesion was situated at the right base, was of mild degree, and was completely recovered from. In one the shadow was certainly due to collapse of the lung and it is concluded that this was the cause of the bronchiectasis. In one other case collapse was the probable cause, and in the third case pneumonic consolidation appeared to be the more likely aetiological factor.

In conclusion, I have pleasure in expressing my indebtedness to Dr. Campbell Suttie, Radiologist at the Royal Hospital for Sick Children, Glasgow, and to Drs. B. J. Leggett and G. Calthrop, Radiologists at the Princess Elizabeth of York Hospital, London, for the various skiagrams reproduced in this paper.

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OSTEOMYELITIS OF THE MAXILLA IN THE NEWLY-BORN

BY

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Osteomyelitis of the maxilla, occurring in the newly-born and in babies up to the age of nine months, is a comparatively rare disease, but the condition has been described in medical literature from time to time, and thirty-six cases have been reported in all. The earliest was reported by Rees in 1847 in a paper dealing with ' Uncommon forms of abscess in children '; in 1897 Sir D'Arcy Power reported a case under the heading, ' Empyema of the antrum in the newly-born '; other writers have described cases under the headings ' Phlegmon of the orbit,' and ' Premature eruption of teeth.' In 1904 Brown Kelly, of Edinburgh, observed a case, and collected together several others. He was probably the first to recognize the lesion as an osteomyelitis of the maxilla.

Case reports.

The typical signs and characteristic clinical picture produced by the disease are well illustrated in the two patients reported here.

Case 1.—R. P., a male child, three weeks old, was brought to hospital because of a swelling in the mouth and a purulent discharge from the gum. There was also great difficulty in feeding the child.

Previous History. The child was born at full term, labour being normal. Birth weight was seven and a half pounds, and the child was breast fed. This was the mother's second pregnancy, the first terminating in a miscarriage at the fourth month. When ten days old the child was noticed to be very irritable, crying frequently, and would not take the breast. The right cheek was swollen and the right lower eyelid puffy. A pale swelling was noticed on the posterior part of the right upper alveolus. When fifteen days old the child was brought to hospital and a rudimentary tooth was removed from the right upper alveolus; this was followed by much purulent discharge from the cavity. Two days later a second rudimentary tooth was spontaneously discharged from the same cavity. The discharge of pus from the alveolus continued, and a purulent discharge from the right nostril followed. Feeding became more difficult and the child was admitted to hospital, being then twenty-four days old.

On Examination, the child was well nourished, and weighed eight pounds and two ounces. The temperature was 99.2° F., pulse

162, and respiration 50. The right side of the face was swollen and oedematous, and the right eye was closed owing to puffiness of the right lower eyelid. There was a purulent discharge from the right nostril. In the mouth a swelling could be seen occupying the posterior part of the right upper alveolus extending outwards toward the cheek and inwards under the muco-periosteum of the hard palate. There was an opening on the gingival margin from which pus could be expressed, and a probe entered for half an inch, rough bone being felt. The swelling on the hard palate was soft and fluctuant. The pre-auricular and cervical glands were enlarged and tender. The heart and lungs were normal. The spleen could not be felt, and there were no other enlarged lymphatic glands. There was a small boil on the back which had been present for one week. The red blood count was 4,660,000 per c.mm., and the white cells 13,000 per c.mm., of which 82 per cent. were lymphocytes. Haemoglobin was 92 per cent.

Two days later a rudimentary tooth and a small fragment of bone were removed from the alveolar margin, and the facial swelling was beginning to subside. Pus continued to discharge into the mouth and from the nose.

When the baby was thirty days old an operation was decided upon. Thirty minims of paraldehyde in half an ounce of saline were given, and produced satisfactory anaesthesia. At the operation the edges of the cavity were avulsed and several small pieces of bone and one rudimentary tooth were removed; the cavity was plugged with adrenaline ribbon gauze, which was removed four hours later. The following day the child was feeding normally at the breast and from the bottle. The discharge of pus quickly dried up and the child made an uninterrupted recovery, leaving hospital three weeks after operation, having gained two and a half pounds in weight. The child has since done well, the alveolar margin has healed, and the face is not sunken. At the age of eight months he weighs nineteen pounds four ounces.

The cultures from the pus grew staphylococcus aureus.

Case 2.—R. W., a male child, aged two months, was brought to hospital because of a swelling of the right side of his face. He had been born prematurely at the seventh month, the mother having had influenza and pneumonia two weeks before delivery. There had been two previous pregnancies, the children being healthy.

When five weeks old the child became irritable. A swelling of the right upper alveolus was noticed, which discharged pus when the mother pressed it. A few days later swelling of the left upper alveolus was noticed and feeding became very difficult.

On Examination the child was well nourished, weighed nine pounds and one ounce. Temperature was 100° F., pulse 152, and respiration 40. There was swelling and oedema of both cheeks and of both lower eyelids. In the mouth there was a tender swelling of the upper left alveolus and a sinus discharging pus in the right upper alveolus. The heart and lungs were normal and the spleen could not be felt. Two days after admission the child developed a swelling on the dorsum of the

right hand, which rapidly spread up the arm to the shoulder and became fluctuant. Temperature rose to 104° F., the pulse to 170, and the respiration rate to 70. The abscess was incised and much pus let out. Seventy c.c. of father's blood was given intravenously, but the child died two days later. Cultures of the pus grew staphylococci in large numbers, and some pneumococci. The Wassermann reaction was negative.

Post-Mortem Examination showed the changes associated with the pyaemic state. There was a purulent pericarditis and there were pyaemic abscesses in the heart muscle. There were small areas of consolidation in the lungs and many small pyaemic abscesses. The liver was pale and soft, the spleen large and soft, and the kidneys showed no changes. In the maxilla there was a small sinus in the right upper alveolus at the site of the unerupted second molar tooth, leading to a cavity lined by granulation tissue and communicating with the middle meatus of the nose. The tooth showed a rough, eroded area. There is no report on the state of the left side. There was an extensive necrosis of the right humerus at the diaphysis, and the periosteum had been stripped up for a considerable length as the result of a large sub-periosteal abscess.

Aetiology.

The disease affects newly-born children. It starts in the first three weeks of life in 90 per cent. of cases, but cases do occur up to the age of nine months. It is now generally accepted to be an osteomyelitis of the maxilla as the result of a blood-borne infection. An empyema of the antrum of Highmore is improbable as this is no more than a shallow groove at birth, measuring ten to twelve mm. in its antero-posterior length and three to four mm. in depth; the opening is along the whole of the lower shelf of the groove. Infection of a dental sac has been suggested as the cause, but it is difficult to decide whether this is primary or secondary. In nearly all the cases reported there was involvement of one or more dental sacs. If these were the primary sites of infection one would expect to find some cases in which the disease process had remained localized. In the majority of cases reported symptoms have pointed to an involvement of the whole bone. This latter fact is strongly in favour of the infection being a true osteomyelitis, with secondary involvement of the dental sacs.

There are many predisposing causes, and among these trauma during birth plays a prominent part. The maxilla at birth is the site of great vascular activity and, being a fixed bone, is very liable to trauma during an abnormal labour. Three cases are recorded following occipito-posterior presentation and three after forceps delivery. Infection of the nasal mucous membrane during passage down the birth canal or injury to the mouth after delivery may be the source of entry for the infection. Cases have been reported associated with areolar infection, mammary abscess, boils, and other sources of focal infection.

Pathology.

In only nine of thirty-six cases is bacteriological evidence available, and in these staphylococcus aureus was present in seven. Streptococci were found in one case and in another tubercle bacilli. French authors have cited syphilis as the cause, but in no case has the Wassermann reaction been positive.

The local lesion in the maxilla probably starts in a blood vessel, either as a direct infection or as a result of a septic embolus. A thrombophlebitis is set up and the vessel becomes occluded, leading to necrosis of the distal parts. Wilensky has made a study of the blood supply of the maxilla, and he regards the slight variations in symptoms as evidence that the initial process has started in one or other of the many branches and vascular loops of the internal maxillary artery. This is substantiated by the cases recorded in the literature, in one of which the entire bone was involved, representing the main trunk artery, while in others the process was localized to the alveolar and nasal branches.

In this connection it may be remembered that the centre of ossification of the maxilla is situated just above the canine and first molar tooth buds. This region is therefore especially vulnerable.

As a result of the necrosis, bony sequestra are frequently formed. If the blood supply of a dental sac is cut off, the rudimentary tooth behaves as a sequestrum, and milk teeth acquire their crown at about the time of the child's birth. This fact helps to establish the time of onset of the disorder when teeth are shed. Following the expulsion of all bony sequestra, healing takes place. Owing to the small amount of periosteum on the maxilla and to its poor nourishment from outside, this process is slow, and new bone formation is frequently incomplete. Locally the disease may progress, causing a secondary nasal infection, a periostitis or a sub-periosteal abscess of the orbit, or a spread may take place through the cribriform plate of the ethmoid, leading to frontal abscess formation. The infection may reach the general circulation leading to pyaemia and the formation of metastatic abscesses. Such abscesses have been recorded in the hand, the shoulder, the pericardium, the heart-wall, the lungs, and the kidneys. In one case reported here a secondary suppurative periostitis of the humerus resulted. Bronchopneumonia may complicate the picture arising as a blood-borne phenomenon, or from aspiration.

Signs and symptoms.

The onset of the disease is mild, there being a few days during which the child is irritable, cries frequently, refuses the breast or bottle, and is generally difficult in management. Fever is not a predominant symptom during this or any other stage of the disease. In only four of the cases reported was pyrexia marked, and in one of these convulsions were observed. Following this prodromal stage, symptoms appear by which the disease may be referred to the maxilla, and they may present at any, or all, of its aspects, namely, orbital, facial, alveolar and palatine, or nasal.

The most common onset is swelling of the face on the effected side with oedema of the eyelid. This was the initial symptom in 70 per cent of cases. Of the remaining cases, the initial symptom in 20 per cent. was swelling of the palate or alveolus, in 9 per cent. profuse nasal discharge, and in one case conjunctivitis and exophthalmos. With the spread of the disease the triad of symptoms, swelling of face and eyelids, discharge from the nostril, and swelling and discharge from the alveolar margin, gives the characteristic clinical picture.

When orbital and facial symptoms predominate there is swelling of the cheek and eyelids, which may cause complete closure of the eyes. With free drainage of the pus the swelling may subside, but in other cases it progresses to abscess formation; such abscesses tend to point at the outer and inferior border of the outer canthus, leaving fistulae, which usually heal after the discharge of dead bone. Conjunctivitis and chemosis are frequently present. Exophthalmos is described in 20 per cent. of cases recorded. It varies from a mild degree to a fairly severe proptosis. When it occurs it is evidence of the spread of the disease to the orbital plate of the maxilla, and is almost certainly caused by a sub-periosteal abscess in the orbit. In no case has the eye itself been affected. Retrobulbar neuritis and optic atrophy do not occur as in ethmoid infection in adults. Glandular enlargement is not mentioned in the cases reviewed, but in one case recorded in this paper the submaxillary and pre-auricular lymphatic glands were enlarged. Retropharyngeal abscess does not occur. Pressure on the swollen face frequently produces an augmented flow of pus from the nostril and alveolar margin, and in one case egg-shell crackling was recorded.

Nasal discharge is the only nasal sign; it may occur at the onset of the disease or during the spread of the infection; it is, as a rule, unilateral, small in amount at onset, becoming profuse as the disease progresses, and it has been recorded as the only residual sign several months after the disease has ceased to be active.

Swelling of the alveolar margin in the region of the canine or first molar tooth is a constant early sign. The swelling may extend on to the hard palate; it is soft and fluctuant, unless it has already burst, leaving an alveolar fistula, through which purulent matter discharges. A rudimentary tooth may be seen as a white plaque on the gums in the region of the swelling. The spontaneous eruption and discharge of such teeth is recorded in the majority of cases, and probably occurs in all cases of the disease. Sequestra are commonly discharged through the alveolar margin; in two cases, however, small pieces of dead bone were extruded from a fistulous opening on the cheek. A probe introduced into an alveolar fistula, enters the dental sac, and frequently communicates with the nose, the thin plate of bone which separates antrum and dental sac being rapidly broken down by the disease process.

The clinical picture is so clear that other aids to diagnosis are hardly necessary, and brief mention only will be made of them. Transillumination has been attempted, but it is unsatisfactory in children. Skiagrams

of the maxillary region are of use in determining the extent of the disease and the presence of sequestra. A mottled appearance is present on the affected side.

Complications.

It would appear from the cases recorded in the literature that the following complications may occur during the course of the disease :—septicaemia (one case with a positive blood culture); pyaemia, with multiple metastatic abscesses in the lungs, kidneys, etc. (two cases); gastro-enteritis; parotitis (one case); cerebral abscess resulting from a direct spread of the disease through the cribriform plate of the ethmoid (one case of frontal abscess); aspiration pneumonia; orbital periostitis and sub-periosteal abscess.

Treatment.

The main objects of treatment are to prevent complications and to attempt to stop the spread of the infection by ensuring free drainage of pus and dead tissues.

The mouth should be cleansed hourly, a solution of 1 in 8,000 permanganate of potash being a suitable disinfectant. Sinuses and cavities in the alveolus should be irrigated with normal saline, and the orifice should be kept open until the discharge of pus has ceased. The child should be nursed on the affected side and, if possible, almost on the face, thus minimizing the risk of aspiration of the pus.

Breast or bottle feeds are not contra-indicated, but should much difficulty arise, gavage feeds can be instituted. It is important to keep the child sufficiently nourished.

The indications for operative measures are :—(1) The presence of abscesses; (2) the progress of the disease, and persistence of purulent discharge; (3) the presence of sequestra and necrosed rudimentary teeth. Abscesses commonly appear on the face or alveolar margin. The latter should be incised as soon as fluctuation is detected; a rudimentary tooth is frequently dislodged during this procedure, which may be followed immediately by a regression of the symptoms after the free discharge of pus. An abscess on the face should be opened early, as damage to the eye may result from delay. Of the cases reviewed, twenty-four were operated on, and in five death occurred. The operations performed varied from the removal of teeth and sequestra from the alveolus to extensive operations on the maxilla. Of the twelve patients not operated on, four died. Wilensky advises operative measures to be as conservative as possible, as extensive operations in acute cases may spread the infection. Exploration of the maxilla by the alveolar route is probably the operation of choice, and this was done in one of the cases reported in this paper. An incision is made into the alveolus on its outer aspect, and the dental sac explored. Rudimentary teeth and dead bone are removed. In most cases a communication between the nose and

mouth will be established, and drainage will be adequate. The cavity should be plugged and the plug removed the following day, when irrigations may be resumed. No attempt should be made to preserve teeth or tooth buds, as these may be responsible for maintaining the infection. In the cases reviewed the majority of operations performed were of this nature, but, in some cases, more extensive explorations were made by a facial route. This does not appear to be a favourable mode of approach, as it must result in permanent disfigurement in later life, while the drainage through such an incision may be hindered by mechanical difficulties.

No mention is made in the cases reviewed of the anaesthetic used. In one of the cases now reported, thirty minims of paraldehyde given in saline per rectum provided adequate anaesthesia.

Prognosis.

The disease must be considered as a serious illness. In the cases reviewed the mortality rate was 26 per cent. The disease may last a few weeks or several months. The formation of sequestra and their gradual extrusion is responsible for delayed healing in many cases, but when these are discharged spontaneously or removed at operation, rapid recovery follows. Future health is in no way impaired. In two cases the face remained sunken on the affected side for some time afterwards, but the disfigurement was only slight. Otherwise the absence of the teeth which have been lost or removed, is the only unpleasant late result.

Summary.

1. Osteomyelitis of the maxilla in the newly-born is a bacterial infection, usually staphylococcal or streptococcal, affecting healthy children between the ages of two weeks and nine months.

2. It is a haematogenous infection localizing in the maxilla, either in the bone itself, in the region of the centre of ossification, or in a tooth bud.

3. The pathology is the same as that for osteomyelitis in older children.

4. The symptoms are clear cut and easily recognized.

5. Some operative measure is indicated in the majority of cases, and should be instituted early.

6. The prognosis is in the first place a serious one, but if improvement follows operation, then a more favourable prognosis may be given.

7. Residual symptoms are few, and a complete recovery is usual.

I am indebted to Dr. Charles Harris and Prof. G. E. Gask for permission to publish these two cases.

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GASTRIC SECRETION IN COELIAC DISEASE

BY

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Coeliac disease is a condition in which the major if not primary disturbance occurs in the alimentary tract. Despite this fact post-mortem observations have revealed little if any morbid change either macroscopic or microscopic in the wall of stomach and bowel. No abnormality of the digestive juices in the small intestine has been recorded. In the stomach, however, there would appear to be some interference with normal function. Marriott[1] found in cases of coeliac disease that there was a marked deficiency of free hydrochloric acid in the gastric juice and that this gradually returned to normal limits as the general health improved. In a series of seven cases Snell and Camp[2] reported the same findings and Parsons[3] has stated that achlorhydria is not uncommon in coeliac disease although free acid can be obtained in response to histamine.

During an investigation into the variations in gastric secretion in infancy and childhood the opportunity was taken to examine seventeen children with coeliac disease. The objects were to determine (a) the free hydrochloric and total acid contents and (b) the peptic activity, and to compare the findings with a group of healthy children who had already been studied[4]. The series here reported included ten girls and seven boys. The ages varied from sixteen months to nine years.

Results.

Details of the individual analyses are given in table 1.

Free hydrochloric acid.—The maximum varied between nil and 63·3 c.c. $\frac{N}{10}$ per cent., with an average of $18{\cdot}0 \pm 3{\cdot}6$. This is significantly lower by $10{\cdot}53 \pm 2{\cdot}66$ than the mean found for the normal group. When first tested, five of the children had hypochlorhydria, two had achlorhydria and one hyperchlorhydria, while the figures for nine fell within the limits of average gastric secretion. The two cases with achlorhydria at the initial test showed no free hydrochloric acid response with histamine. One of these, five months later, gave a moderately good result with the ordinary test meal while the

* This work was done during the tenure of a Muirhead Scholarship and a McCunn Medical Research Scholarship.

other, four months later, still had achlorhydria but gave a good response after injection of histamine. It is clear, therefore, that in this series there was no case of true achlorhydria. The boy with hyperchlorhydria was undoubtedly the subject of coeliac disease. He presented the typical clinical and biochemical picture, the absorption of fat was found to be very defective and both his height and weight were well below the average for his age.

TABLE 1.

GASTRIC ANALYSIS (MAXIMUM FIGURES) IN COELIAC DISEASE.

NAME.	AGE IN YEARS.	SEX.	HCl. C.C. $\frac{N}{10}$	TITR. ACID C.C. $\frac{N}{10}$	TOTAL CHLORINE C.C. $\frac{N}{10}$	PEPTIC ACTIVITY UNITS.
J.R. ...	$1\frac{4}{12}$	F.	16·9	25·4	86·8	—
C.B. ...	$2\frac{2}{12}$	M.	22·2	61·2	89·5	52·9
W.McK.	$2\frac{6}{12}$	M.	20·0	35·0	68·1	25·6
M.O'B. ...	$2\frac{6}{12}$	F.	*nil.	7·5	61·0	10·0
	$2\frac{10}{12}$		nil.	21·4	78·8	—
			*44·0	56·0	103·5	40·0
P.S. ...	$2\frac{10}{12}$	F.	nil.	10·0	84·2	67·6
			* nil.	23·5	110·2	—
	$3\frac{3}{12}$		18·5	27·8	83·6	25·6
			* 8·3	22·4	67·8	67·6
J.W. ...	$2\frac{11}{12}$	F.	7·5	22·0	80·1	115·6
D.McL.	$3\frac{3}{12}$	M.	14·9	30·0	101·0	40·0
	$3\frac{6}{12}$		nil.	21·4	90·5	52·9
B.S. ...	$3\frac{6}{12}$	F.	12·0	60·0	78·5	12·1
J.C. ...	$3\frac{8}{12}$	M.	21·5	36·8	101·3	25·6
G.B. ...	4	M.	8·7	23·8	71·2	14·4
	$4\frac{2}{12}$		17·5	27·0	84·2	40·0
H.B. ...	$4\frac{6}{12}$	F.	2·2	35·6	75.7	22·5
			* nil.	41·7	77·4	84·1
	$4\frac{7}{12}$		4·4	21·1	71·9	2·5
M.H. ...	$4\frac{10}{12}$	M.	63·3	73·3	87·4	67·6
J.J. ...	6	F.	39·4	52·5	109·0	22·4
B.McA.	7	F.	22·5	32·8	68·8	62·5
H.A. ...	8	F.	21·7	47·4	70·4	25·6
J.J. ...	8	F.	21·7	73·6	118·8	32·4
J.M. ...	9	M.	12·0	28·0	64·9	—
	$9\frac{2}{12}$		25·6	35·9	82·3	102·4

* AFTER HISTAMINE.

In the hope of showing some relationship between the hydrochloric acid secretion in the gastric juice and the nutritional condition of the patients the percentage of expected weight was plotted in each case against the figure for maximum hydrochloric acid secretion. There did not appear to be any correlation. This is perhaps to be expected since weight is to a considerable degree dependent on the height which in turn depends in great part on the previous retention of minerals. Clearly before any marked increase of weight can occur there must be improvement in the general condition, and it is probable that the state of well-being of the patient at the time of the test has an influence on the gastric secretion. This view is supported by the present findings. Six of the children were re-examined some months later, when the general health had improved and they were gaining weight (table 2).

TABLE 2.

CHANGES IN GASTRIC ANALYSIS WITH IMPROVEMENT OF HEALTH.

NAME.	AGE IN YEARS.	SEX.	DATE TESTED.	EXP. WEIGHT. PER CENT.	HCl c.c. $\frac{N}{10}$	TITR. ACID. c.c. $\frac{N}{10}$	TOTAL CHL. c.c. $\frac{N}{10}$	PEPTIC ACT. UNITS.
M.O'B. ...	$2\frac{6}{12}$	F.	30. 6.33	60·06	*nil	7·5	61·0	10·0
	$2\frac{10}{12}$		13.10.33	64·05	nil	21·4	78·8	—
			17.10.33		*44·0	56·0	103·5	40·0
P.S. ...	$2\frac{10}{12}$	F.	9. 6.33	46·07	nil	10·0	84·2	67·6
			12. 6.33		*nil	23·5	110·2	—
	$3\frac{5}{12}$		21.11.33	63·10	18·5	27·8	83·6	25·6
			22.11.33		*8·3	22·4	67·8	67·6
D.McL. ...	$3\frac{5}{12}$	M.	21. 3.33		14·9	30·0	101·0	40·0
	$3\frac{6}{12}$		23. 6.33		nil	21·4	90·5	52·9
G.B. ...	4	M.	6. 4.33	87·14	8·7	23·8	71·2	14·4
	$4\frac{2}{12}$		30. 5.33	90·39	17·5	27·0	84·2	40·0
H.B. ...	$4\frac{6}{12}$	F.	13. 3.34	42·49	2·2	35·6	75·7	22·5
			16. 3.34		*nil	41·7	77·4	84·1
	$4\frac{7}{12}$		24. 4.34	46·85	4·4	21·1	71·9	2·5
J.M. ...	9	M.	4.11.32	44·21	12·0	28·0	64·9	—
	$9\frac{2}{12}$		5. 1.33	45·02	25·6	35·9	82·3	102·4

* AFTER HISTAMINE.

In four the percentage of free hydrochloric acid in the gastric juice was raised. In one of these four the free hydrochloric acid increased from 12·0 to 25·6 although the percentage of expected weight had risen from 44·2 to 45·0. It would appear, therefore, that the secretion of hydrochloric acid in coeliac disease bears some relationship to the state of the patient at the time the test is made but not to his state of nutrition.

The number of the cases in the series is too small to make any reliable statements on the effect of age on the gastric hydrochloric acid but it is of

interest to note that here, as in normal children, there is evidence of increased ability to secrete hydrochloric acid in the older children (table 3).

TABLE 3.

MAXIMUM VALUES FOR COELIAC AND NORMAL CASES IN AGE PERIODS.

AGES.	NO. OF CASES.	FREE HCl C.C. $\frac{N}{10}$			TOTAL ACIDITY C.C. $\frac{N}{10}$			TOTAL CHLORINE C.C. $\frac{N}{10}$			PEPTIC ACTIVITY UNITS.		
		LOW.	HIGH.	AVER.	LOW.	HIGH.	AVER.	LOW.	HIGH.	AVER.	LOW.	HIGH.	AVER.
0—3 YEARS.													
COELIAC ...	6	nil.	22·2	11·1	7·5	61·8	26·8	61·0	89·5	78·3	10·0	115·6	54·3
NORMAL ...	12	6·7	50·0	22·7	33·5	66·0	43·9	68·4	93·9	75·9	22·5	96·1	50·1
3—6 YEARS.													
COELIAC ...	6	2·2	63·3	20·4	23·8	73.3	43·2	71·2	101·3	85·8	12·1	67·6	30·4
NORMAL ...	19	12·5	55·7	30·0	31·1	75·0	46·0	57·0	95·5	79·2	6·4	108·9	50·9
6—9 YEARS.													
COELIAC ...	5	12·0	38·4	23·4	28·0	73·6	46·8	64·9	118·8	86·4	22·4	62·5	35·7
NORMAL ...	15	19·9	56·6	31·4	30·3	90 7	50·7	52·5	104·3	77·1	—	—	32·4*

* ONLY ONE CASE.

Total acidity.—The maximum figures for total acidity varied between 7·5 and 73·6. The mean value for the whole group was $38·5 \pm 4·8$, being $8·48 \pm 1·62$ lower than that for the control series, a result which is not statistically significant for the number of cases investigated. (In the older children the maximum total acidity was higher.) It would appear, therefore, that the total acidity is not affected to such a marked degree as the free hydrochloric acid, indicating the formation of organic acids in the gastric juice.

Total chlorine.—The maximum total chlorine of the gastric contents varied between 61·0 and 118·8, the mean value being greater by $5·69 \pm 1·3$ than that of the control group. These figures would suggest that it is only the mechanism concerned with the production of free hydrochloric acid which is at fault and not that which governs the secretion of chlorides. Nor can the argument be put forward that neutralization was the cause of diminished free hydrochloric acid since no evidence of regurgitation of duodenal contents was obtained and the occurrence of bile in the gastric contents was not more frequent than in the normal series. The increase of neutral chlorine is probably to be attributed to the increased concentration of blood chloride, the mean value of which was $82·68 \pm 1·54$, i.e. $8·91 \pm 4·43$ higher than in the

control group (table 4). An explanation of this latter finding is to be sought in the anaemia which is so common in coeliac disease giving rise to a relative increase in the volume of plasma which contains much more chlorine than the corpuscles.

TABLE 4.

BLOOD ANALYSIS OF CASES OF COELIAC DISEASE AND NORMALS.

	0–3 YEARS.		3–6 YEARS.		6–9 YEARS.	
	COELIAC.	NORMAL.	COELIAC.	NORMAL.	COELIAC.	NORMAL
NO. OF CASES	7	21	5	18	3	15
AVERAGE TOTAL CHLORINE. c.c. $\frac{N}{10}$	83·58	73·73	81·43	73·74	82·66	73·90

Peptic activity.—The maximum peptic activity varied from 10·0 to 115·6 units with a mean value of 42·1, which was similar to the average figure obtained in the control series. The upper limit, however, was much lower in the coeliac group.

Emptying time.—The average was found to be slightly longer than in the control group. The gastric contents still contained traces of the test meal at two hours in six cases.

Conclusions.

The results of gastric analysis of the series of seventeen cases of coeliac disease recorded in this communication confirm the findings of other workers that there is impaired secretion of free hydrochloric acid in the stomach but that true achlorhydria does not occur. There was no diminution in peptic activity but a slight prolongation was noted in the emptying time. The total chloride was increased, a finding which is presumably the result of the greater concentration of chloride in the blood, which is to be attributed to the decrease in red cell count and increase in plasma. The hypochlorhydria is probably an important aetiological factor in the production of hypochromic anaemia in patients with coeliac disease.

An increase in the gastric secretion of free hydrochloric acid was noted as the general condition of the patient improved and as the bulk and composition of the faeces became more normal.

I desire to thank Prof. G. B. Fleming and Dr. N. Morris for suggesting this investigation and for their helpful criticism and Dr. Shepherd Dawson for his help in the statistical portion of the work. I also wish to acknowledge the gift by Messrs. Parke, Davis and Co. of the histamine phosphate used in the cases referred to in this paper.

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CARCINOMA OF THE THYROID GLAND IN CHILDHOOD

WITH REPORT OF A CASE

BY

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Malignant growths of the thyroid gland have been well studied recently, but their occurrence at ages below 20 or 30 remains rare and interesting. It is generally agreed that the fourth to sixth decades are those in which carcinoma is most usually met; in the literature there are only a small number of cases reported under the age of 30, and it seems to be exceptional under the age of ten. The present case occurring at the age of six is, therefore, of some interest, especially as it caused difficulty in diagnosis owing to the predominant features of the pulmonary metastases.

Hughes[1], in 1920, reported a case occurring in a girl of 13 who had had a mid-line swelling in the neck for three years, but with no obstructive symptoms. A group of glands was removed from the right side of the neck and showed replacement by papilliferous carcinoma. The thyroid tumour was then removed with difficulty and showed the same changes. Three months later the child was well. Blaxland[2] operated on a girl of 25 who had had the right lobe of her thyroid removed when 19 for a parenchymatous goitre which was confirmed microscopically. He excised the left lobe for further pressure symptoms and section then showed the presence of adeno-carcinoma in one area. A year later the patient was well. Schultz[3] records a case of a girl of five-and-a-half years. Atypical thyroid tissue of highly malignant character had invaded the capsule, surrounding tissue and lymph-nodes. The child was still well nineteen months after removal of the tumour and roentgen irradiation. He emphasizes the facts, also mentioned in Hughes' paper, that this type of neoplasm seems less malignant and less liable to infiltrate than the similar growths of older persons. Ewing[4], in an extensive discussion of the pathology of the condition, gives the general age of 50-60 as the usual one, and extremes of 10-90, but quotes a case recorded by Demme in a boy of five. In 1929 specimens were shown at the Royal Society of Medicine by Moncrieff[5] from a girl of 11, who had been under the care of Dr. F. J. Poynton. She had been noticed to have a swelling in the neck since the age of four, but only in the last few months had it enlarged

and caused noisy respiration. An operation was attempted owing to urgent obstructive symptoms, but adhesions, especially to the deep layers, caused difficulty and the child died soon after. On microscopical examination of the superficial parts of the gland typical parenchymatous goitre was seen, but deeper there were definite malignant changes, partly papilliferous, partly solid carcinoma, with infiltration of the trachea, and other structures. Cattell[6, 7] has recorded four cases in children. The first of these, in a girl of eleven years, had lumps in the right side of her neck which had appeared one-and-a-half years previously. Nine months before a biopsy had shown non-malignant glands, but six months subsequently it was repeated and thyroid papillary-cystadenoma was found. A radical dissection was carried out, including the jugular vein, and the right lobe and isthmus of the thyroid itself. The histology was confirmed, and post-operative x-ray treatment was given. A year later the patient was healthy. He also had another case in a girl of eleven years with nodules of papillary-cystadenoma in an aberrant thyroid and one lobe of the main gland. She, too, was well two years after eradication associated with x-ray therapy. In another case growth was found in the wall of a thyroglossal cyst in a boy of six, who was well fifteen months after its surgical removal. The fourth case is more like the case to be described here, and that reported by Poynton and Moncrieff. A boy of 13 developed a hard mass in one lobe of the thyroid, shortness of breath, respiratory wheeze and stridor. The trachea, by x-rays, was seen to be deviated and narrowed. A highly malignant, small-celled carcinoma, histologically resembling lymphosarcoma, was removed and x-ray therapy was given, but recurrences appeared in the chest and the boy died. Dunhill[8] reported the occurrence of lateral, aberrant thyroid nodules in the neck of a patient of sixteen, who was known to have had lumps there since he was twelve. The thyroid was enlarged, but quite separate. Microscopically the nodules consisted of papilliferous growth into cystic spaces, some of which contained colloid. He classed them as papillary-cystadenomata, with a tendency to undergo malignant transformation. Griffith and Mitchell[9] emphasize the rarity of these tumours in children, but note that aberrant thyroid tissue may develop tumour masses and cysts, into which class of case those of Cattell and Dunhill can be included. Pemberton and Dixon[10] in a paper summarizing the end-results of treatment of various forms of malignancy, mention the age incidence of 323 cases of thyroid malignancy, of which two are under nine, and eight more between ten and nineteen. It is possible that here are included malignant tumours, other than carcinoma, such as sarcoma, which may occur less rarely in childhood. Lee[11] reported a case of carcinoma of the thyroid in a child of eight years. Schreiner and Murphy[12], in a paper on malignant neoplasms of the thyroid, have investigated some of the literature on cases occurring in younger patients. They cite eight cases below the age of 30, but only half of these are under 20: Bérard[13] reported the condition in a girl of eighteen, Müller[14] in a boy of eighteen, Meleney[15] in a boy of seventeen, and Hughes' case, already mentioned, in a girl of thirteen.

These reports show that carcinoma of the thyroid does occur in childhood, but that it is unusual and arouses special interest. All the authors and other authorities are agreed that it is usually to be considered a disease of persons over 40. In a few of these cases quoted the condition has arisen in aberrant masses of thyroid tissue in the neck, and several have emphasized a pre-existing goitre, as sometimes occurs at the later ages.

Pathology.

From the pathological point of view these growths fall into two groups. In one they seem to run a relatively benign course and the malignant nature may only be found after histological examination, infiltration and glandular invasion not having been seen at operation. A number of these have been referred to, and operation combined with x-ray therapy has mainly given good results within periods up to a year or two. On the other hand, some of the cases, notably that described by Poynton and Moncrieff, Cattell's fourth case and our case, described below, are of much more rapid evolution with infiltration of the trachea, neck tissues and glands, producing respiratory obstruction. Operation, often in a rather vain hope, is difficult and unsatisfactory. These cases run a much more rapid course, and by the time a diagnosis can be arrived at and treatment considered it is already too late. Death from asphyxia or exhaustion, due to partial asphyxia, occurs, while the general nutrition remains little impaired.

Another interesting difference between the two groups is in regard to metastases. Whereas in the one the growth has remained local, the other often shows at autopsy multiple metastases, and in this conform to the adult type. The lungs are particularly susceptible, and secondary deposits may be either large and few or small and disseminated. The occurrence of the latter type in our case, appearing radiologically very like miliary tuberculosis, caused much difficulty in diagnosis before the mass in the thyroid became visible, palpable or remarkable by its symptoms. The ready invasion of the veins and lymphatics so closely in relation to the rapidly infiltrating growth is given as the usual explanation of the early appearance of metastases and their wide distribution. Ewing states the order of frequency of these in 238 cases was : lungs, bones, liver, kidneys, pleura, brain and elsewhere. There is a plate in his book of a skiagram to show multiple pulmonary metastases of miliary type, similar to the one of our case reproduced here, though showing less isolation of the multiple foci.

Histologically, the classification of primary thyroid carcinomata at all ages has been clarified by Joll[16], who divides them into three groups :—

(1) malignant adenoma; (2) papilliferous carcinoma; and (3) carcinoma simplex.

Most of these reported cases in children appear to fall into one of the first two groups and it appears significant that those which by their reports are of the adenomatous type, are also of that group—less malignant, more localized and with a better prognosis—described above. On the other hand where a papilliferous carcinoma has been found the other, much more serious group seems to correspond, with early infiltration and metastasis. The case reported here is of this type and the microphotographs and pathological report are typical of this growth. The case reported by Poynton and Moncrieff was illustrated by a microphoto-

graph showing this type though also in parts there was solid carcinoma. A point of interest in connection with the metastases is that they may function as normal thyroid tissue after thyroidectomy although microscopically they may appear either non-malignant or similar to the original growth.

Case history.

The patient, a well-built girl of six years and three months, came to the out-patient department of the Belgrave Hospital for Children in May,

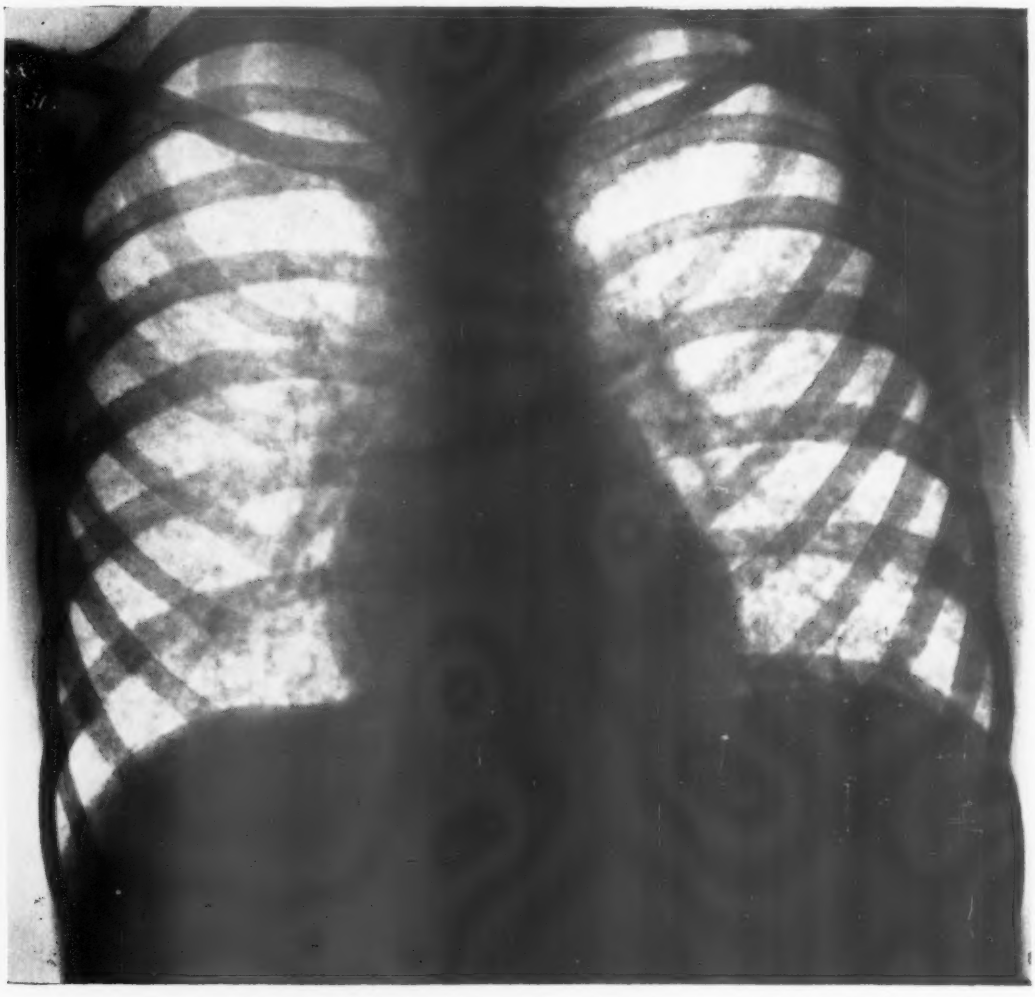

FIG. 1.—X-ray picture of lungs showing miliary metastatic deposits.

1931, complaining of a cough of five weeks' duration following a cold. There was some shortness of breath and occasionally a little expectoration, but never haemoptysis. Her general health had not altered though she had not been strong since an attack of food poisoning a year before.

Examination revealed only the presence of a number of small, discrete,

hard glands in the neck, and in view of the cough the chest was x-rayed, revealing appearances suggestive of miliary tuberculosis (fig. 1). The patient was therefore admitted to hospital on May 21. The cough had, by then, become more of a hoarse bark occurring in paroxysms and there was persistent shortness of breath.

The child preferred to sit up in bed; her breathing was harsh and noisy with an occasional dry, barking cough. Examination of the lungs

FIG. 2.—Skiagram of neck showing distortion of trachea by primary growth in thyroid.

showed mainly abdominal respiration with hollowing of the sternum. The resonance was high pitched and breath sounds were harsh, accompanied by scattered râles. The liver was palpable, but not enlarged, and the spleen was not felt. In the neck a number of firm, discrete glands were present on both sides in relation to the sterno-mastoids. The thyroid

gland then felt normal. The temperature was subnormal and pulse between 80 and 110, respirations 24 to 28. Her weight was 37 lb. 14 oz.

On June 8, the child was still apparently well though her breathing was hoarse. No gross abnormal signs were found in the chest and the glands in the neck remained hard and discrete. A Mantoux tuberculin reaction was carried out and was negative. At this point the diagnosis presented a considerable problem. The diminution of the cough, absence

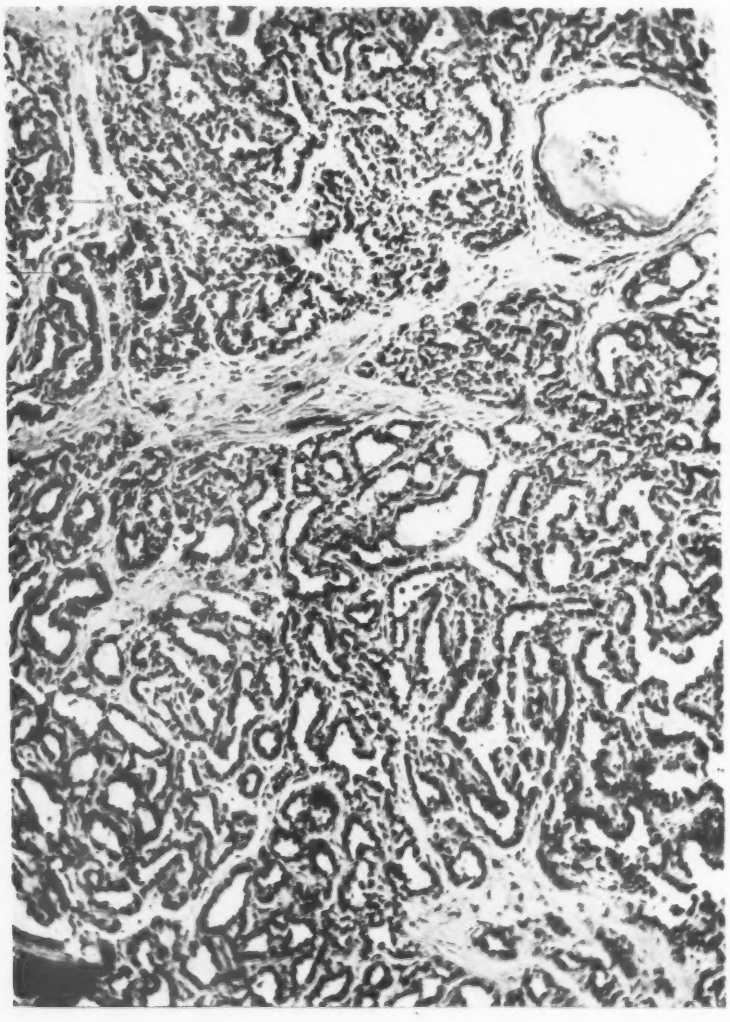

FIG. 3.—Section of growth in thyroid × 125.

of sputum and temperature and the fact that the child was not in herself ill discredited the x-ray suggestion. Moreover the smallness of the glands and the absence of palpable thyroid changes did not attract attention thereto and the pulmonary condition, even in the absence of physical signs, was the centre of interest.

By July 1, however, some alterations had occurred. Dyspnoea had become more marked and was accompanied by stridor. This appeared to be due to tracheal obstruction and a skiagram (fig. 2) showed narrowing and distortion of the upper part of the trachea. The cervical glands were also increasing. She was seen by Mr. Negus at King's College Hospital, and he confirmed the tracheal obstruction and considered that it was due to glandular enlargement which extended down into the

FIG. 4.—Section of bronchial gland × 125.

mediastinum. At this point lymphadenoma and lymphosarcoma were suggested as possible diagnoses, although no other glands or the spleen could be felt.

The glands were fusing into a thick mass on both sides of the trachea and larynx, and dyspnoea was becoming more acute. The blood count

showed 7,010,000 red corpuscles per c.mm. and 125 per cent. haemoglobin. The leucocytes were 24,000 per c.mm. During the last few days before death on July 16 her condition was distressing; orthopnoea occurred in attacks and was increasingly severe. Between attacks she recovered extraordinarily and would take nourishment. The fact that her weight was almost unaltered since admission showed how little general disturbance

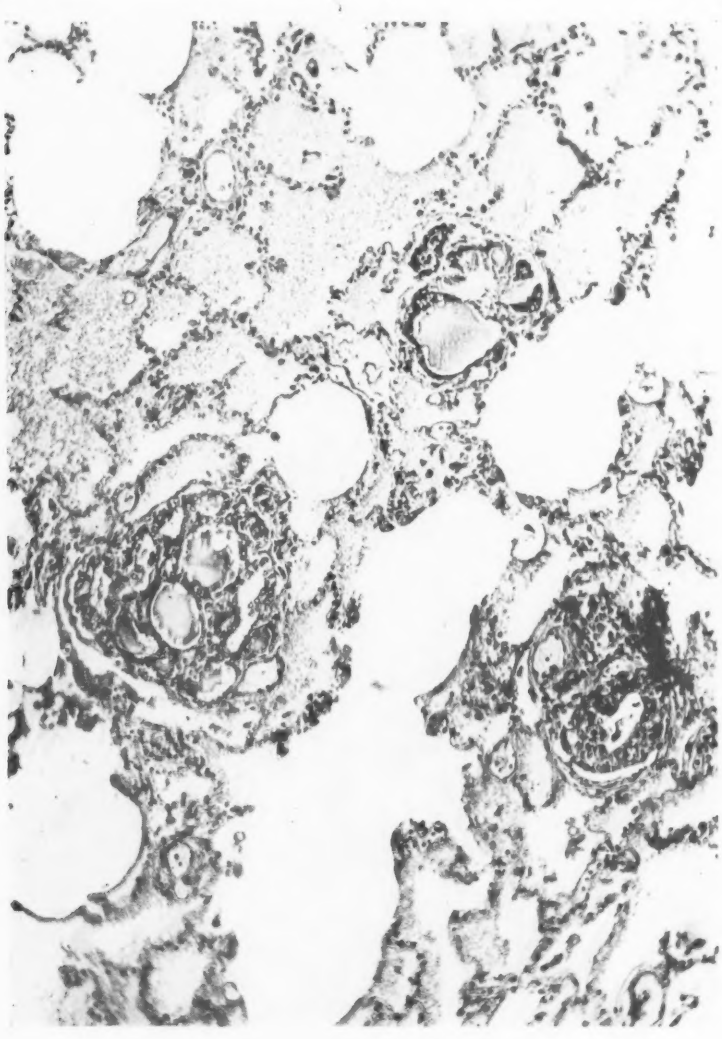

FIG. 5.—Section of metastasis in lung × 125.

there was apart from the mechanical obstruction to breathing. Finally she died of asphyxia.

The skiagrams reproduced show the miliary metastatic deposits throughout the lungs very similar to those of miliary tuberculosis, and also the glandular enlargements at the hilum and in the mediastinum. The narrowing and distortion of the trachea can be seen extending as low as the fifth cervical vertebra.

A post-mortem examination was carried out; the body was that of a well-nourished girl and a mass of glands was palpable round the trachea; no other enlarged glands were felt. The thyroid was completely enclosed anteriorly; posteriorly it was found that both lobes were hard and enlarged, especially the right, and measured about 2½ inches across. It was adherent to the trachea and on making sections the lumen was found to be occluded partly by invasion and partly by compression, mainly at the level of the second and third rings, causing thereby the fatal asphyxia. The heart was normal except for dilatation of the right ventricle. The lungs were studded throughout with hard white nodules of growth varying in size from a pin's head to a pea. There was no evidence of caseation and apart from engorgement the lung substance was otherwise normal. In the neck there was a mass of enlarged glands round the upper part of the trachea, extending from the level of the larynx to the sternal notch and continued on, less extensively, into the bronchial glands. The glands were discrete, hard and of a uniform consistency. Some were the size of a walnut, but most were smaller. There was dense fibrous tissue between them. All the other organs were normal.

Histology. Much of the growth was similar to normal thyroid tissue, with abundant colloid formation. In other parts the vesicles became very irregular, containing papillary processes, and the colloid scanty (fig. 3). In a few places the cells were in masses, giving the appearances of a solid carcinoma. The cells were atypical cubicle or tending to columnar. The growth on the right side was invading the outer layer of the trachea. It appeared to be of the type of papillary carcinoma of Joll's classification.

CERVICAL GLANDS.—These were extensively invaded by malignant growth. There was no collloid formation (fig. 4).

LUNGS.—There were numerous deposits of thyroid carcinoma. Many of these reproduced the structure of a normal thyroid very accurately with colloid formation (fig. 5).

Summary.

The rarity of carcinoma of the thyroid in children is noted and a review of the literature is given. Two groups of cases appear to occur: one relatively benign and slow growing and more usually of adenomatous type histologically; the other rapidly malignant, readily metastazising and of papilliferous type histologically.

An example of this second type in a girl of six years is described in detail, in which the multiple pulmonary metastases seen by x-rays before the original growth became evident strongly suggested miliary tuberculosis, but later when this was clinically untenable the thyroid tumour appeared and caused rapid respiratory obstruction with death from asphyxia four months after the first symptoms of the illness.

We are indebted to Dr. Oddy for permission to publish the notes of the case.

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BLOOD TRANSFUSION IN THE MALNUTRITION OF INFANCY

BY

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The treatment of the marasmic infant is not the least difficult of the many perplexing problems which confront the paediatrician. If cases showing evidence of organic disease and those where the feeding is either unsuitable or mismanaged be excluded, there are still those infants whose constitution is such that neither skilful feeding nor expert nursing can coax them along the highroad to health. Such children are the despair of both parent and doctor. It is for these infants that blood transfusion is a worthy adjunct to routine methods, as illustrated by the following results. Used as an emergency measure in the extreme stages of enteritis, the results are often disappointing. The fact that one such patient, apparently moribund when transfused, is now a healthy baby, demands that all measures be tried even when the cause seems lost. The group of cases where blood transfusion was employed soon after the onset of enteritis show distinctly favourable results.

When the condition of malnutrition remained uncomplicated, blood transfusion led to an immediate and sustained gain in weight. These infants had failed to respond to routine treatment over a long period. No addition to the treatment was made either following the transfusion or for some days previous to it. Five patients with severe enteritis died. All the others to whom blood was given have subsequently done well. The results afford evidence that in most cases blood transfusion does supply a stimulus to the marasmic infant. The precise nature of the stimulus is not clear. Blood transfusion may act (a) by supplying physiological fluid; (b) by supplying a deficiency of one or more of the solid contents of the blood; and (c) by exciting a tissue response in the bone marrow or elsewhere.

Once the marasmic infant ' turns the corner,' the subsequent prognosis is favourable. These results are presented, with the belief that blood transfusion may supply that added stimulus which sets the infant on the path to recovery. No suggestion is made that blood transfusion should replace routine methods.

Carefully performed, blood transfusion is a procedure devoid of risk. In this series there were no unfavourable reactions or sequelae. In most of the cases one of the parents acted as donor, and in every case the recipient's serum was tested directly against the donor's corpuscles. The serum and corpuscles were left in contact for twenty minutes before a decision was made on the compatability of the bloods. In two instances the baby's serum agglutinated the mother's corpuscles and one of these was a baby aged six weeks—an indication of how early in life the blood groups may be distinctly differentiated.

Method

The blood was obtained from the donor by means of a large-bore needle which had previously been washed through with sterile sodium citrate solution. A suitable vessel containing a quantity of 3·8 per cent. sodium citrate solution received the blood, which was then put aside in a basin containing warm water and gently stirred until required. One part of citrate solution was used for nine parts of blood. On one occasion a specimen containing this proportion of citrate and blood was set aside for twenty-four hours. At the end of that period the whole quantity was passed, without difficulty, through a fine hypodermic needle. The syringe used to transfer the blood from the container to the vein was of the Jubé pattern with a barrel capacity of 5 c.c. It may be noted that for this type of work the gravity method is entirely unsuitable, as it requires too great a head of pressure to run the blood into the small vein of an infant. A blunted hypodermic needle was employed for insertion into the recipient's vein in place of a cannula. The whole apparatus was washed through with citrate solution and laid aside ready for use.

Exposure of the vein.—A short length of the internal saphenous vein was dissected out at the ankle under local anaesthetic and a temporary ligature tied at the lower limit of dissection. A second, loosely tied ligature was placed round the vein at the upper limit of dissection. The vein was then incised longitudinally to avoid the risk, inherent in a transverse incision, of a complete division. The apparatus was then filled with blood, the cannula inserted into the vein and the transfusion begun.

When the required amount had been transfused the cannula was withdrawn and both ligatures removed. The skin incision was sutured and haemorrhage controlled by a pad and bandage over the wound. By this method an attempt was made to avoid permanent occlusion of the vein.

As it was considered advisable that the blood be given slowly, a minimum period of fifteen minutes was set for the transfusion of the blood, however small the quantity used. For this reason, the indirect method was used exclusively in the younger infants, the direct method being employed in older children.

Definite rules cannot be laid down as to the quantity of blood given. On an average 10 to 15 c.c. per pound of body weight forms a safe guide. In cases showing extreme degrees of dehydration larger quantities may be given with safety. In babies who are malnourished rather than dehydrated the lower limit is probably best.

The results are embodied in the following tables and certain cases are described individually.

Group 1. Cases complicated by severe enteritis.

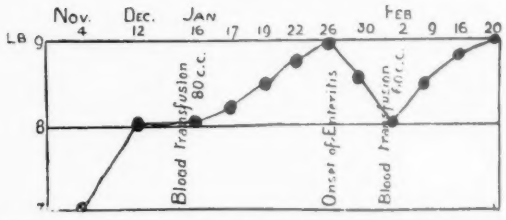
(Blood transfusion performed as an emergency measure).

Case no.	Age in weeks	Weight on admission lb.	Weight on admission oz.	Period between admission and onset of enteritis in days	Period between onset of enteritis and blood transfusion in days	Amount of blood : c.c.	Result
1	4	5	1	8	6	90	Death
2	7	6	6	15	2	75	Death
3	12	7	4	Enteritis on admission	3	60	Death
4	5	4	14	23	3	100	Death
5	12	7	12	21	10	50	Death
6	5	6	0	36	5	75	Recovery
Averages	8	6	3	17	5	57	—

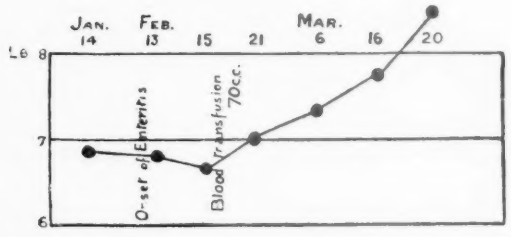
Death occurred at an average of sixty hours after transfusion.

Following transfusion in case 6, vomiting was completely arrested and the stools improved progressively. There was no marked gain in weight until seven weeks later when lactic acid and Nestlé's feeds were instituted. Eleven weeks after operation the baby was discharged weighing 9 lb. 6 oz. The result in this case was dramatic.

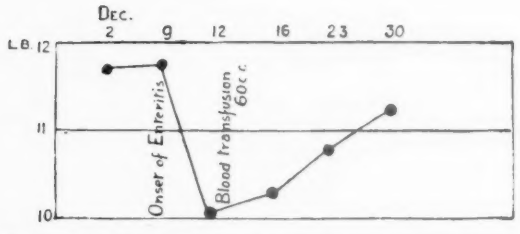
Group 2. (A) Cases complicated by enteritis of less severity.



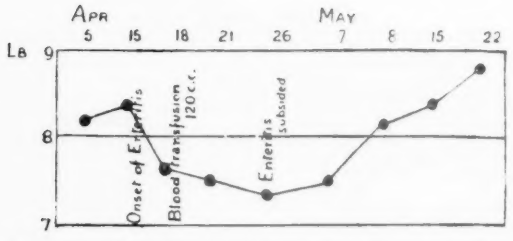
CASE 7.—MALNUTRITION, AGED THREE WEEKS.
Subsequent progress satisfactory.



CASE 8.—MALNUTRITION, AGED SIX WEEKS.
Subsequent progress satisfactory.

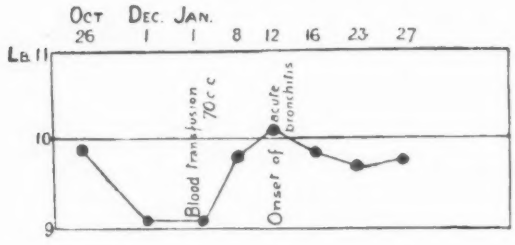


CASE 9.—MALNUTRITION, AGED FOUR MONTHS.
Subsequent progress satisfactory.



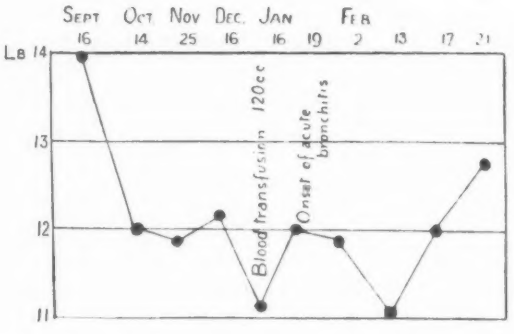
CASE 10.—MALNUTRITION, AGED ELEVEN WEEKS.
This case appeared to derive no benefit from blood transfusion. Progress followed subsidence of the enteritis and the addition to the the feeds (milk and water) of Benger's. Subsequent progress satisfactory.

Group 2. (B) Cases complicated by other conditions.



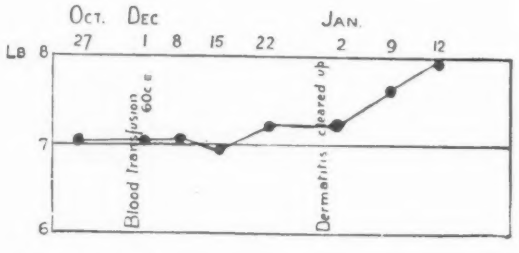
CASE 11.—MALNUTRITION, AGED FIVE MONTHS, COMPLICATED BY ACUTE BRONCHITIS.

Subsequent progress satisfactory. The attack of bronchitis caused a temporary check in the progress following transfusion.



CASE 12.—MALNUTRITION, AGED SEVEN MONTHS, COMPLICATED BY ACUTE BRONCHITIS.

Improvement following transfusion checked by onset of acute bronchitis. Subsequently made good progress.



CASE 13.—MALNUTRITION, AGED SIX WEEKS, COMPLICATED BY CHRONIC DERMATITIS.

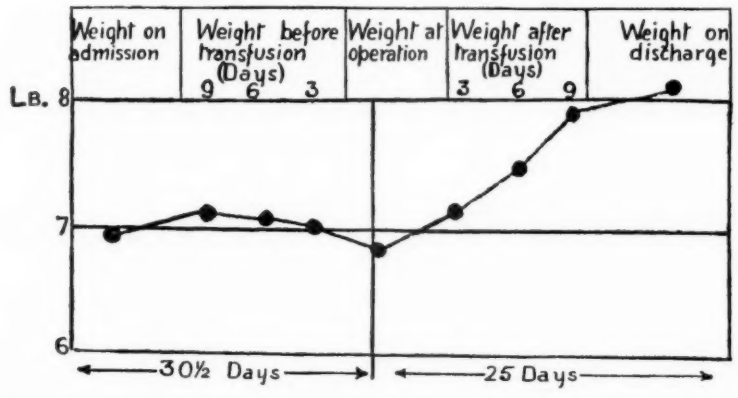
Blood transfusion did not appear to benefit this case. Subsequent progress satisfactory.

Group 3. Uncomplicated cases of malnutrition.

Case no.	Age in weeks.	Period between admission and transfusion in days	Amount of blood given in c.c.	Admission weight lb.	Admission weight oz.	Weight at operation lb.	Weight at operation oz.	Discharge weight lb.	Discharge weight oz.	Gain per day after operation in oz.
14	7	24	70	5	2	5	4	6	10	0·88
15	24	52	110	12	2	11	10	12	14	0·66
16	7	33	120	5	6	5	4	6	6	0·82
17	10	17	110	7	8	7	6	8	10	1·05
18	5	44	60	6	4	6	12	7	6	0·71
19	10	21	65	5	8	5	6	7	4	0·88
20	9	47	70	6	0	6	4	7	10	0·59
Averages	8	30½	85	6	15	6	11	8	1½	0·8

In all these seven cases, the gain in weight after operation was sustained and the starting point coincided with the operation. The average period from operation to discharge was twenty-five days.

Composite weight chart of the above cases.



In the normal child the average gain in weight in the first twelve months is four ounces per week. In these seven cases the gain per week from operation to discharge was five-and-half ounces.

Survey of results.

If a gain in weight is taken as the criterion of improvement, blood transfusion was successful in twelve of the twenty cases. Excluding the five

fatal cases there were a further two cases where no apparent benefit followed. In these it is impossible to assess what part transfusion played. In case 6, despite the fact that no gain in weight followed the operation, the clinical improvement was so impressive as to leave no doubt, in the minds of those associated with the case, that transfusion had been a life-saving procedure. The results in uncomplicated cases of malnutrition (group 3), are suggestive, without being entirely conclusive. Proof must await trial in a large number of cases. It is suggested that blood transfusion is a remedy of value in uncomplicated cases of chronic malnutrition.

Summary.

(a) In the advanced stage of acute enteritis blood transfusion should be a routine measure. A favourable response can be expected only in a small proportion of such cases.

(b) In the marasmic infant, blood transfusion should be employed as soon as the condition of acute enteritis supervenes.

(c) In uncomplicated cases of malnutrition blood transfusion is a valuable measure. A favourable response may be expected in a large percentage of such cases.

I am indebted to the Honorary Medical Staff of the Royal Manchester Children's Hospital for their kind permission to publish these results.

THE RED CORPUSCLES IN ACIDOSIS AND ALKALOSIS

BY

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As far back as 1895, Gurber, Hambürg and v. Limbeck showed that the addition of carbon dioxide to the blood caused increase in the volume of the red cells. Price-Jones[1] in his investigations into the diameter of the red corpuscles found that there is a diurnal variation, the cells being smaller in the morning and larger later in the day, when the alkalinity is less. He further noted that violent exercise, by increasing the accumulation of lactic acid, and thereby causing lessened alkalinity of the blood, is accompanied by increase of cell diameter, and that in the converse state of increased blood alkalinity, produced by hyperventilation, which drives off carbon dioxide from the blood, there is a diminution of cell diameter. Experiments in vitro, blood being made more or less alkaline, produced corresponding results.

In these instances the change in acid-base equilibrium was transient. Similar findings, however, have been described when the disturbance was of longer duration. Földes[2], Holler and Kulka[3] noted an increase in the volume of the red corpuscles in diabetic coma, the first showing that treatment with alkali caused a return to normal. Wiechmann[4] observed an increase in cell volume with return to normal during treatment with insulin. Increased cell volume, with decreased cell diameter, was however described by Holler and Kulka[3], the cells apparently becoming globular in shape, and Horwitz[5] made similar observations in experimental acidosis produced by calcium chloride. Increase of cell diameter occurs in the deep sleep induced by the administration of morphine (Wiechmann and Shürmeyer[4]). The same workers describe diminution of mean diameter of the red corpuscles after administration of sodium bicarbonate.

An increase in red cell count in diabetic coma is described by Grawitz (quoted by Horwitz) and by Földes, the latter being of the opinion that the erythrocytosis is directly proportional to the severity of the acidosis. Detre and Zárday[7] found erythrocytosis in experimental acidosis produced in dogs. The former observed an increase in the red cell count after strenuous work. This did not occur when alkali was given.

In the following study, Price-Jones curves were constructed from cases of acidosis and alkalosis occurring in children. The blood of ten children was examined. Four of these were examples of acidosis, two

with diabetic coma and two with acidosis produced by calcium chloride. Six were examples of alkalosis and included two of subacute nephritis undergoing treatment with massive doses of sodium bicarbonate, and four of congenital hypertrophic pyloric stenosis. The technique followed in construction of the curves was that described by Price-Jones[1]. Blood films, made on slides and dried by air, were fixed with Jenner's stain and counter-stained with watery eosin. A projection apparatus was used in drawing the cells, the magnification being 1,000 diameters. The cells were measured in two directions at right angles, the square root of the product, to the nearest 0.25μ, being taken as the mean diameter of the corpuscle. In the construction of a curve five hundred cells were measured.

The blood in acidosis.

Table 1 summarizes the results found in acidosis. It will be seen that in all four cases there was an increase in corpuscular diameter (shift

TABLE 1.

THE EFFECT OF ACIDOSIS ON THE RED CORPUSCLES.

Case No.	Nature of Case	Hb. per cent.		R.B.C. in millions per c.mm.		M.C.D. (μ)*		Shift to right (μ)	Blood CO_2 (Vol. per cent.)
		During Acidosis	On Recovery	During Acidosis	On Recovery	During Acidosis	On Recovery		
1	Diabetic coma	106	95	5·64	4·96	7·459	6·745	0·714	27·8
2	Diabetic coma	—	—	—	—	7·752	7·146	0·606	—
3	Calcium chloride acidosis	78	76	4·46	4·38	7·468	7·079	0·389	11·8
4	Calcium chloride acidosis	50	50	4·00	3·94	6·731	6·099	0·632	21·5

*M.C.D. = Mean corpuscular diameter.

to the right), but that this was not proportional to the diminution of blood carbon dioxide. Furthermore, the shape of the curves was not changed, the whole being moved *en masse* to the right in each case. Examples of this are shown in fig. 1 and 2. In three of the four cases it was found that the coefficient of variation was decreased during acidosis. Erythrocytosis occurred in diabetic coma, but in neither of the cases of calcium chloride acidosis.

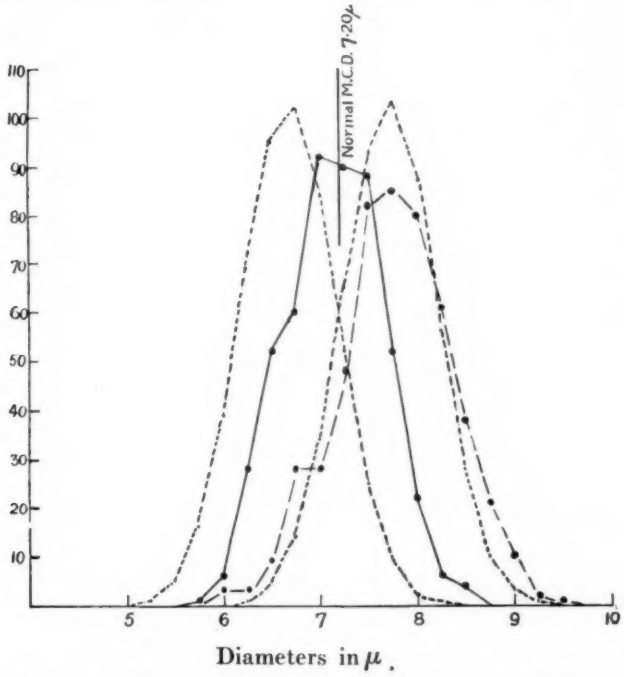

FIG. 1.—Price-Jones curves in a case of diabetes, during coma (broken line) and on recovery (continuous line). Mean diameter during coma 7·752μ. Mean diameter on recovery 7·146μ.

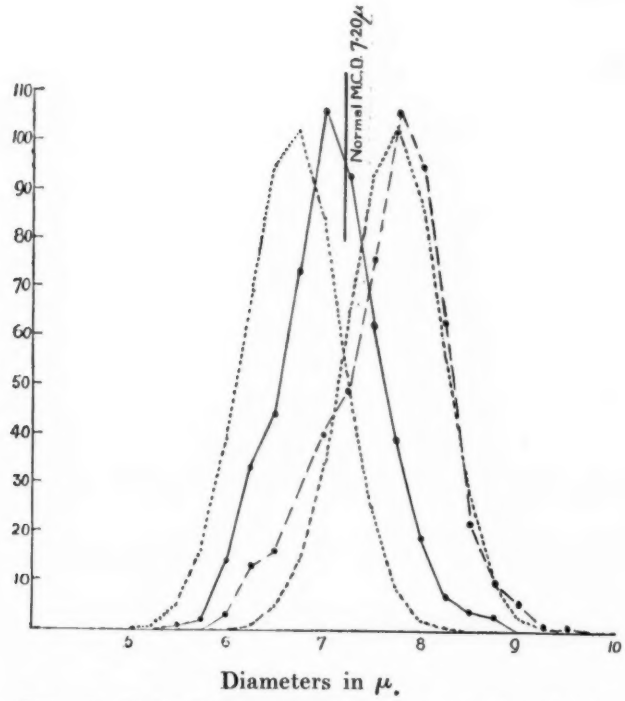

FIG. 2.—Price-Jones curves in a case of acidosis produced by administration of calcium chloride. Mean diameter during acidosis (broken line) 7·468μ; mean diameter on recovery (continuous line) 7·079μ.

The blood in alkalosis.

The findings in alkalosis produced by the administration of sodium bicarbonate in nephritis are found in table 2. Here there was a diminution in red cell diameter during alkalosis, though the general characters

TABLE 2.

THE EFFECT OF ALKALOSIS ON THE RED CORPUSCLES.

Case No.	Nature of Case	Hb. per cent.		R.B.C. in millions per c.mm.		M.C.D. (μ)*		Shift to left (μ)	Blood CO_2 (Vol. per cent.)
		During alkalosis	On recovery	During alkalosis	On recovery	During alkalosis	On recovery		
5	Alkali administration in subacute nephritis	80	76	4·14	4·12	6·041	7·242	1·201	82
6	Alkali administration in subacute nephritis	90	85	4·87	4·61	6·706	7·381	0·675	—

*M.C.D. = Mean corpuscular diameter.

of the Price-Jones curve were unchanged, as shown in fig. 3. In these cases the coefficient of variation was increased in the alkalotic period.

No change in the erythrocyte count was noted in either case.

Cell volume was estimated in case 6. Blood, oxalated by the method described by Wintrobe[8] in America and by Vaughan and Goddard[9] in England, was centrifugalized in graduated centrifuge tubes, and not in the haematocrit as was done by these workers. Mean corpuscular volume (M.C.V.) of the red cells is given in cubic μ, mean corpuscular haemoglobin content (M.C.H.) in micro-microgrammes of haemoglobin ($\gamma\gamma$) and mean corpuscular haemoglobin concentration (M.C.H.C.), i.e., the haemoglobin per unit volume of red corpuscle, as a percentage. Table 3 shows that the volume of the red cells in alkalosis was reduced and, though the total amount of haemoglobin remained unchanged, its concentration was increased, i.e., fluid had been removed from the cells.

In pyloric stenosis it is well recognized that there is a state of alkalosis. Clinically this is manifested by the slow respiratory rate, which has been shown to bear a close relationship to the blood carbon dioxide[11]. In the four cases examined there was a definite diminution in the mean cell diameter, but this did not appear to be proportional to the degree of alkalosis as gauged by the respiratory rate. The data are given in table 4, where the normal cell diameter for the age, as determined by van Creveld[10] is also shown. The Price Jones curve has the characteristic broad base of curves at this age (fig. 4). Marked erythrocytosis was present in all four cases.

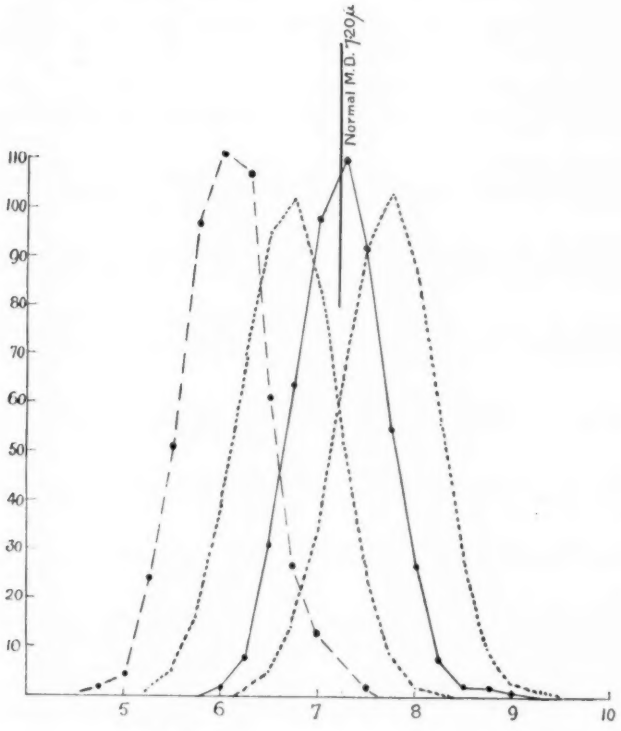

FIG. 3.—Price-Jones curves during alkalosis produced by the administration of sodium bicarbonate. Mean diameter during alkalosis (broken line) 6·041 μ ; mean diameter on recovery 7·242μ.

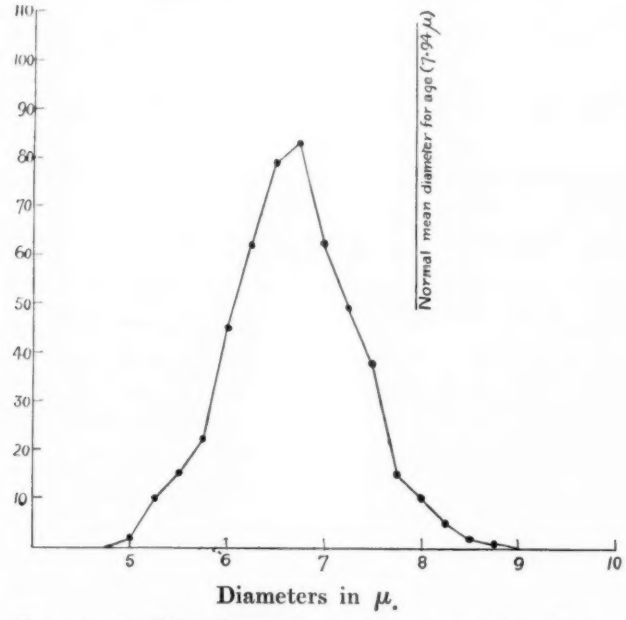

FIG. 4.—A Price-Jones curve in a case of pyloric stenosis in a child aged five weeks, mean diameter 6·68μ. The normal mean diameter at this age (7·94μ) is also shown.

TABLE 3.

THE INFLUENCE OF ALKALOSIS ON THE VOLUME AND THE HAEMOGLOBIN OF THE RED CELLS.

	R.B.C. in millions per c.mm.	Hb. in gm. per cent.	Vol. of packed R.B.C. per cent.	M.C.V. in c. μ	M.C.H. in $\gamma\gamma$	M.C.H.C. per cent.
Average for five normal normal children ...	5·17	13·02	40·60	78·54	25·17	32·07
Case 6. (During alkalosis) ...	4·87	12·69	33·5	68·78	26·05	37·88
Case 7. (On recovery) ...	4·61	11·59	39·0	84·59	25·14	29·72

M.C.V. = Mean corpuscular volume.
M.C.H. = Mean corpuscular haemoglobin.
M.C.H.C. = Mean corpuscular haemoglobin concentration.

TABLE 4.

THE INFLUENCE OF THE ALKALOSIS OF PYLORIC STENOSIS ON THE RED CORPUSCLES.

Case No.	M.C.D. (μ)	Normal M.C.D. for age (μ)	Shift to left (μ)	Respiratory rate per min.	Blood count.
7	7·28	7·94	0·66	32	Hb. 100 per cent. R.B.C. 4,800,000
8	7·68	7·94	0·26	28	Hb. 105 per cent. R.B.C. 5,300,000
9	6·68	7·94	1·26	22	Hb. 135 per cent. R.B.C. 6,800,000
10	7·33	7·72	0·39	28	Hb. 110 per cent. R.B.C. 5,500,000

M.C.D. = Mean corpuscular diameter.

Discussion.

Detre was of the opinion that acid stimulated erythropoiesis, but Horwitz[6] points out that there is no evidence of this, as the number of reticulocytes is normal throughout acidosis and states that though on account of the reduction of blood volume in diabetic coma there may be an apparent erythrocytosis, the total number of red cells in the body is the same as when acidosis is absent. The increased red cell count in acidosis is therefore probably due to blood concentration, but erythrocytosis is not an invariable finding, as it occurred in neither of our cases of acidosis due to calcium chloride. In diabetes progressing to coma there is always great loss of fluid, while this is not a notable feature in cases of acidosis produced by calcium chloride, a fact which would explain the absence of erythrocytosis in our two cases of the latter.

All the results obtained by separating corpuscles from plasma, by centrifugalizing oxalated blood, are in agreement that in acidosis the ratio of red cells to plasma is increased. Horwitz, and Holler and Kulka, who hold that there is no increase in the mean diameter, maintain on the basis of this finding that the individual cell undergoes a change of size and shape, becoming more globular. The data on which Horwitz based this conclusion are more readily explained by the presence of anhydraemia due to loss of fluid. It would be necessary before concluding that the red cells enlarge by assuming a globular shape without increase in diameter to prove that the increase of the volume of packed cells in the centrifugalized blood was greater than could be explained by decreased plasma volume.

In our series, however, an increase of cell diameter occurred in both diabetic coma and acidosis from calcium chloride administration, and in the latter no change in red cell count was present, proving that while the blood plasma may or may not be decreased, there is certainly an increase of corpuscular size, though the shape of the cell is not apparently changed.

These results are parallel with the findings of Price-Jones in transient non-gaseous acidosis, and Wiechmann and Shürmeyer in gaseous acidosis, and show in contrast to the results of other workers, that in prolonged pathological non-gaseous acidosis the same changes occur. It may be that in addition to the anhydraemia the increased size of the corpuscle increases the viscosity of the blood, and so plays a part in the circulatory failure which so frequently accompanies grave acidosis.

We have been unable to demonstrate any correlation between the extent of increase of cell diameter and the diminution of blood carbon dioxide, although the latter is not necessarily an exact measurement of the degree of acidosis.

It is of interest to note that case 4 had a marked microcytic, hypochromic anaemia, which did not modify the behaviour of the cells in acidosis.

Alkalosis has the reverse effect on the red corpuscle, causing a reduction in its volume, and its mean diameter. The haemoglobin content remains unchanged, but the concentration of haemoglobin per unit volume of red cell rises. This effect is doubtless due to the removal of water from the corpuscle. There is no change in the erythrocyte count in alkalosis produced by sodium bicarbonate.

Price-Jones found that the coefficient of variation was increased in acidosis and suggested that possibly some cells were more sensitive to change in acid-base equilibrium than others. In three of our four cases the coefficient of variation was decreased in acidosis. These apparently

conflicting results might be explained for, if, as Price-Jones suggests, some cells are more sensitive than others it would take longer for the less sensitive cells to be affected and it would only be when they had been subjected to acidosis for some time that an increase in size would occur.

In the two cases of alkalosis produced by sodium bicarbonate the variability was increased. This may be due to unequal sensitivity of the cells, and to the fact that conditions necessitating withdrawal of cellular fluid were not so urgent as those demanding the converse movement, which occurs in acidosis. For lack of data regarding the normal variability in the distribution of the cells of young infants, it is impossible to say whether there was any variation from normal in the cases of pyloric stenosis examined. In pyloric stenosis there is increase in the cell count from blood concentration, due to vomiting and inadequate intake of fluid.

In early infancy the diameter of the red cells is much greater than in older children and adults. The red cells probably attain normal size about the sixth month and certainly in the first year. In spite of these differences, a microcytosis occurs in alkalosis, but there again there is little correlation between the degree of alkalosis as estimated by the respiratory rate, which is recognized to be proportional to the amount of carbon dioxide in the blood.

Price-Jones has suggested that carbon dioxide is the immediate factor in producing changes in cell size. Since increase in cell diameter occurs both in gaseous and in non-gaseous acidosis, and decrease both in gaseous and non-gaseous alkalosis, it cannot be either the free or the total carbon dioxide which is the factor, but rather the ratio of the free to the combined carbon dioxide, i.e., the cell size varies as the pH of the blood, increasing with decreased pH and vice versa.

Summary and conclusions.

In acidosis, whether occurring in disease or induced by drugs, the red corpuscles are enlarged, the cell apparently retaining its normal shape. This may be accompanied by an increase in the red cell count, which, when it occurs, is probably due to blood concentration.

It is suggested that the increase in cell size in addition to the anhydraemia may be a further cause of increased blood viscosity, and may contribute to the tendency to circulatory failure in acidosis.

Alkalosis causes a reduction in the size of the corpuscles, without change in shape, or haemoglobin content. There is probably no change in the red cell count due to alkalosis per se.

The corpuscles in early infancy, in spite of their different features, react to alkalosis in the same way as those of the older individual.

I have pleasure in recording my gratitude to Prof. G. B. Fleming and Dr. N. Morris for their valuable criticism and advice, and to the Rankin Medical Research Fund for financial assistance.

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